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TABLE OF CONTENTS FIRST PAGE

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CONTENTS

Original Articles

Roentgenological Findings in Tuberous Sclerosis — PAGE
Harry I. Berland, M.D., St. Louis 669

Language Behavior in Psychoneurotic Patients
Maria Lorenz, M.D., and Stanley Cobb, M.D., Boston 684

Prognosis of Neurologic Illness Following Vaccination Against Smallpox
Henry G. Miller, M.D., F.R.C.P., Newcastle upon Tyne, England 695

Electroencephalograms of Nonepileptic Psychotic Patients Awake and Asleep
George Lyketsos, M.D.; Louis Belinson, M.D., and F. A. Gibbs, M.D., with the Technical Assistance of Anton Engel, Chicago 707

Psychodynamics in the Excessive Drinking of Alcohol
John W. Higgins, M.D., New Haven, Conn. 713

Effect of Mephenesin upon Anxiety
Stanley L. Block, M.D., Norfolk, Va. 727

Xanthochromia of the Cerebrospinal Fluid
R. M. N. Crosby, M.D., Baltimore, and Glenn L. Weiland, Ph.D., Gettysburg, Pa. .. 732

Thiamylal in Electroconvulsive Therapy and Significance in Analysis of Seizure Mechanisms
Ralph S. Green, M.D., and Rudolf Leiser, M.D., Eloise, Mich. 737

Electroencephalographic Findings Associated with Subdural Hematoma
Ernst A. Rodin, M.D.; Reginald G. Bickford, M.B., and Hendrik J. Svien, M.D., Rochester, Minn. 743

Wilson's Disease (Hepatolenticular Disease)
Frank L. Sullivan, M.D.; Herbert L. Martin, M.D., and Fletcher McDowell, M.D., New York 756

Case Reports

Photogenic Epilepsy: Parameters of Activation
C. Marshall, M.D.; A. Earl Walker, M.D., and S. Livingston, M.D., Baltimore 760

March of Piloerection as a Convulsive Equivalent
William M. Landau, M.D., St. Louis 766

Society Transactions

Chicago Neurological Society 769

New York Neurological Society and New York Academy of Medicine, Section of Neurology and Psychiatry 772

Philadelphia Neurological Society and Philadelphia Society of Anesthesiologists 775

Regular Departments

Abstracts from Current Literature 778

News and Comment 790

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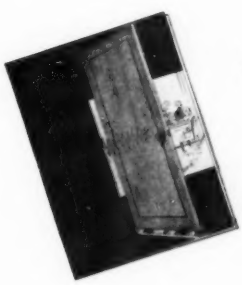

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ROENTGENOLOGICAL FINDINGS IN TUBEROUS SCLEROSIS

Bone Manifestations

HARRY I. BERLAND, M.D.
ST. LOUIS

TUBEROUS sclerosis is a rare disease due to an abnormal development of the germinal layers primarily involving the ectodermal structures. Bourneville [1] first described this disease in 1880. He referred to the skin eruption as "acne rosacea" and demonstrated sclerotic areas in the brain at autopsy. The commonest clinical findings are mental deficiency, convulsions, and adenoma sebaceum. This syndrome is referred to as epiloia.[2]

Marcus, cited by Dalsgaard-Nielsen,[3] is credited as being the first, in 1924, to describe the roentgenologic changes in tuberous sclerosis. His findings were limited to the skull, and he spoke of layers of "chalk shale" and calcifications the size of a bean being found on roentgenological examination of the skull. Later, in 1935, Dalsgaard-Nielsen [3] demonstrated that these calcifications were sclerotic plaques within the skull. Gottlieb and Lavine,[4] in 1935; Kveim,[5] in 1937; Pancoast, Pendergrass, and Schaeffer [6]; Hueblein, Pendergrass, and Widmann,[7] Ackermann,[2] and others reported various osseous lesions in this disease.

It is difficult to determine the exact number of cases that have been reported in the literature. Freeman, cited by Ferraro and Doolittle,[8] in 1922 estimated that approximately 100 cases had been reported up to that time. He pointed out that cases of tuberous sclerosis had been reported under various other names because of

1. Bourneville, D.: Scléreuse tubéreuse des circonvolutions cérébrales: idiotie et épilepsie hémiplégique, Arch. neurol. **1**:81-91, 1880.

2. Ackermann, A. J.: Pulmonary and Osseous Manifestations of Tuberous Sclerosis, with Some Remarks on Their Pathogenesis, A. J. Roentgenol. **51**:315-325 (March) 1944.

3. Dalsgaard-Nielsen, T.: Tuberous Sclerosis with Unusual Roentgen Picture, Nord. med. tidsk. **10**:1541-1548 (Sept. 28) 1935.

4. Gottlieb, J. S., and Lavine, G. R.: Tuberous Sclerosis with Unusual Lesions of the Bones, Arch. Neurol. & Psychiat. **33**:379-388 (Feb.) 1935.

5. Kveim, A.: Über Adenoma sebaceum (Morbus Pringle), und seinen Platz im neurokutanen Syndrom—tuberöse Gehirnsklerose—und dessen Beziehung zur v. Recklinghausenschen Krankheit: Drei Fälle von tuberöser Sklerose und Morbus Pringle mit röntgenologisch nachweisbaren Veränderungen in Cerebrum und im Knochensystem, und Tumorbildungen in Retina, Acta dermat.-venereol. **18**:637-683 (Oct.) 1937.

6. Pancoast, H. K.; Pendergrass, E. P., and Schaeffer, J. P.: The Head and Neck in Roentgen Diagnosis, Springfield, Ill., Charles C Thomas, Publisher, 1940, p. 663.

7. Heublein, G. W.; Pendergrass, E. P., and Widmann, B. P.: Roentgenographic Findings in the Neurocutaneous Syndromes, Radiology **35**:701-727 (Dec.) 1940.

8. Ferraro, A., and Doolittle, G. J.: Tuberous Sclerosis (Diffuse Neurospongioblastosis), Psychiatric Quart. **10**:365-416 (July) 1936.

the bizarre nature of the disease. A review of the literature shows that 361 cases have been reported since 1922. The purpose of this paper is to add five new cases to the literature and to review three others in which the roentgenographic findings in the hands and feet were not reported originally.

Almost every organ and structure of the body has been reported to have been involved in this disease. In 80% of the cases pathologic changes have been described in the brain or kidney [9] as demonstrated either roentgenologically or at autopsy; these are the best-known lesions in the disease. In 65% of the cases roentgenographic changes have been shown in the hands or feet; these lesions are not well known. A roentgenologic diagnosis can be established by correlation of the x-ray findings in the skull and those in the hands or feet; no other disease presents this association.

Microscopic examination of decalcified sections of bone shows thick trabeculae within the cancellous bone.[3] The calcium content is low, with few cells visible within the bone spaces. Diffuse fibrous tissue, also poor in cells, is seen within these spaces, giving the appearance of cystic changes. Hyalinized connective tissue in irregular layers, producing some fragmentation of the cortex, is seen toward the surface of the bone.[2]

The commonest ectodermal lesions are those observed in the brain. Smooth, firm nodules of various shapes and sizes are seen on the surface. These also may be found in the walls of the ventricles, producing the characteristic "candle gutterings" frequently demonstrable in ventriculograms. Grossly, the sulci and gyri show no deformity. Microscopically, there are giant nerve cells in both the gray and the white matter. The pyramidal cells are decreased and the Cajal cells are increased in number. There also are patchy and coalescent areas of destruction of the myelin sheaths. Wertham, cited by Ross and Dickerson,[10] believed that the disorganization occurs in the fifth and sixth months of gestation. Nodules are frequently seen in the fundus of the eye; they may be multiple or single and often resemble a cluster of grapes. These were first called "phakomas" by van der Hoeve.[11] Mesodermal involvement usually results in tumor formation. Tumors have been described in every organ of the body. The renal tumors are of the mixed embryonal type.

The incidence of the disease is estimated to be about 0.0002% of the general population,[10] about 0.1% of the admissions to institutions for the care of the feebleminded and epileptic [12] in America, and about 0.6% of such admissions in Europe.[12] The disease may be hereditary or familial, and the sex distribution is equal. The three patients whose cases are reviewed were all siblings from one family.

Clinically, the disease may first manifest itself in infancy or in adult life. In one case the presenting symptom occurred at the age of 49.[12] A mild or major convulsion may be the first symptom. Skin lesions of acneiform type are not present in

9. Mertz, H. O.: Tuberous Sclerosis and Renal Tumor, Tr. Am. A. Genito-Urin. Surgeons **35**:73-85 (May) 1942.

10. Ross, A. T., and Dickerson, W. W.: Tuberous Sclerosis, Arch. Neurol. & Psychiat. **50**:233-257 (Sept.) 1943.

11. van der Hoeve, J.: Eye Symptoms in Phakomatoses: The Doyne Memorial Lecture, Tr. Ophth. Soc. U. Kingdom **52**:380-401, 1932.

12. Dickey, L. B.: Tuberose (Tuberous) Sclerosis or Epiloia, Stanford M. Bull. **7**:74-77 (May) 1949.

infancy, since the sebaceous glands are not developed; however, adenoma sebaceum develops with the appearance of the sebaceous glands. The skin lesion may resemble a fine acne rosacea, assuming a butterfly distribution over the face, or it may be a large, confluent, resilient tumor of the skin. The latter type of lesion may be painful in cold weather. Other skin lesions are pigmented nevi; large areas of pigmentation, most commonly found over the sacral region; filiform papillomas of the nail beds; pedunculated polyps, and subcutaneous nodules. It is rare to make a diagnosis without the skin lesions. Almost all patients are mentally retarded and may frequently become behavior problems. Occasionally, however, such patients may present normal mentality and good insight. Other findings frequently encountered are spina bifida, polydactyly, harelip, cleft palate, renal tumors, visual disturbances due to phacomas and cardiac anomalies.

The roentgenographic findings of calcifications within the brain is well known; however, less attention has been given in the literature to the osseous changes which occur in this disease. Roentgenographic findings in the bony structures of the hands and feet may be divided into three groups: (1) cyst-like changes in the phalanges with or without osteoporosis; (2) irregular cortical thickening of the metatarsals, metacarpals, or phalanges without active periosteal reaction, and (3) a mixed type, consisting of cortical thickening with fragmentation.

REPORT OF CASES

The first group, of three cases, illustrates the small cyst-like areas found in the phalanges, usually the distal phalanges, with or without osteoporosis.

CASE 1.—M. K. was the oldest of three siblings with tuberous sclerosis reported by Goodfriend.[13] He demonstrated the roentgenologic changes in the skull but did not take roentgenograms of the hands or feet. The patient, a 13-year-old white girl, had had convulsions in early infancy. At 2 years of age there developed a papular eruption with a butterfly distribution over the face; she presented a behavior problem, but at no time had she shown evidence of mental retardation.

The patient was well developed, well nourished, and cooperative on examination. There was a fine papular eruption over the bridge of the nose, the cheeks, and the upper and lower lips. Several areas of hyperpigmentation and depigmentation were seen scattered over the body. The left eye showed a deep optic cup and prominent cribriform plate. Vision was impaired in the left eye; the right eye was essentially normal. The rest of the physical examination showed an essentially normal condition. She had an intelligence quotient of 95, which was consistent with average intelligence, and she was doing well in her school work.

Posteroanterior and right lateral views of the skull showed several fleecy areas of calcifications within the cranial vault in the parietal region (Fig. 1 *A*). The bony architecture, vascular channels, suture lines, and sella turcica were normal. Anteroposterior views of the hands showed round "punched-out" areas of decreased density, some measuring about 4 mm. in diameter, in the tips of the distal phalanx of both index fingers, right ring finger, and left thumb and in the middle phalanx of the right ring finger and both little fingers (Fig. 1 *B*). Similar areas of decreased density were seen in the distal phalanx of both great toes (Fig. 1 *C*). There was no zone of sclerosis about these "cystic" lesions. The rest of the bones and epiphyses appeared normal.

CASE 2.—A. S., a white man aged 40, was referred to Dr. L. V. Mulligan for repair of a bilateral, indirect inguinal hernia by the State of Missouri Welfare Agency. Unfortunately, a complete psychiatric history was not obtained, but the following facts were established. He was

13. Goodfriend, J., in discussion on Friedman, R.: Tuberous Sclerosis, Clinical Conference, J. Pediatrics **32**:589-594, 1948.

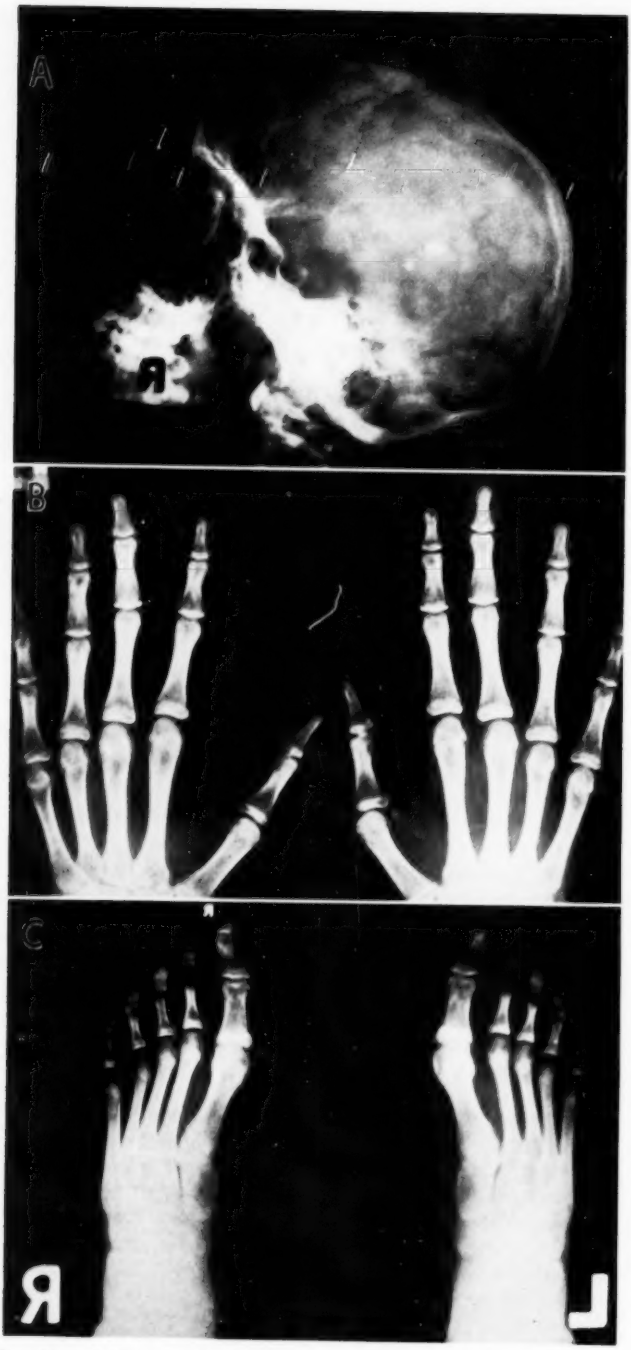

Fig. 1 (Case 1).—*A*, fleecy calcifications within the cranial vault. *B*, cyst-like lesions without a surrounding zone of sclerosis in the phalanges of both hands. *C*, cyst-like lesions in the distal phalanx of both great toes. The lesion in the distal phalanx of the right great toe is irregular and has a zone of sclerosis around it.

mentally retarded and had not done well in school; he finished the sixth grade but could advance no further. As far as could be determined, he had never had convulsions. He was able to do menial tasks and was employed part time. At the time of admission he was working on a delivery truck as truck driver's assistant.

Physical examination revealed a large bilateral indirect inguinal hernia; this condition has since been repaired. Attention was called to the skin lesions on his face, which were described as "warty blemishes." This led to investigation of the skull and hands, which definitely established the diagnosis of tuberous sclerosis.

Roentgenograms of the skull revealed irregular bilateral calcifications within the brain in the middle cranial fossa (Fig. 2). The bony architecture of the skull appeared normal; there was no evidence of thickening of the tables or patchy areas of sclerosis. Roentgenograms of the hands showed a punched-out, cyst-like area, about 3 mm. in diameter, with a thin zone of sclerosis in the tip of the distal phalanx of the right ring finger. A smaller cyst-like area without a zone of sclerosis was observed in the base of this phalanx. Another "cyst" was observed at the base of the proximal phalanx of the right thumb; it lay near the surface and produced an escalloped effect. Two small "cysts" were present in the distal half of the distal phalanx of the left index finger and the left middle finger, and a single one was present in the tip of the

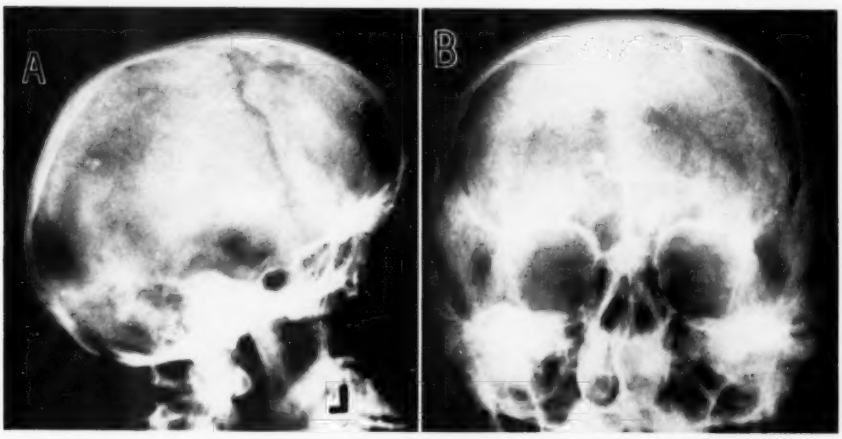

Fig. 2 (Case 2).—Calcifications within the cranial vault. They are sharply outlined, dense, asymmetrical, and of various sizes.

distal phalanx of the little finger (Fig. 3). No other findings referable to tuberous sclerosis were noted in the remaining bones of the hands or wrists.

Case 3.—R. B., a white boy aged 13, was mentally retarded. He had an intelligence quotient of 31. He presented a behavior problem in that he had violent temper tantrums, but there was no history of convulsions.

On physical examination he appeared well developed and well nourished, but was uncooperative. He had a fine papular eruption on the bridge of the nose, spreading laterally over the cheeks. There also was a subcutaneous nodule, about 2 cm. in diameter, over the lower lumbar region. The rest of the physical examination revealed nothing significant.

Lateral roentgenograms of the skull revealed a cluster of calcifications in the middle cranial fossa and some thinning of the inner table of the frontal bone (Fig. 4*A*). The rest of the skull appeared normal. Roentgenographic examination of the left hand showed a small "cyst" in the tip of the distal phalanx of the index finger with a zone of surrounding sclerosis (Fig. 4*B*). The remaining bones of the hand appeared normal.

These cases demonstrate the cystic type of change observed in the phalanges of the hands and feet. The lesions appeared to be more abundant in the phalanges of

the hands and were either intramedular or adjacent to the cortex. Occasionally one might be seen near the surface of the cortex, as demonstrated in the proximal phalanx of the right thumb in Case 2 (Fig. 3). Similar-appearing cystic changes may be present in the following diseases: 1. Recklinghausen's disease, or neurofibromatosis. In this condition there are multiple areas of bone absorption with true cyst formation. The cysts, if large, may be trabeculated and occur anywhere within the diaphysis. There may also be thinning of the cortex with or without expansion of the bone shaft. 2. Polyostotic fibrous dysplasia. In this disease there are usually multiple areas of bone absorption or destruction, presenting cyst-like lesions of various sizes unassociated with any considerable demineralization of bone. 3. Enchondroma. This lesion is usually multiple and predominates in the bones of the hands and feet, producing localized expansion of the shaft of the bone, without proximity to the epiphyses. 4. Gout. This condition produces rounded punched-

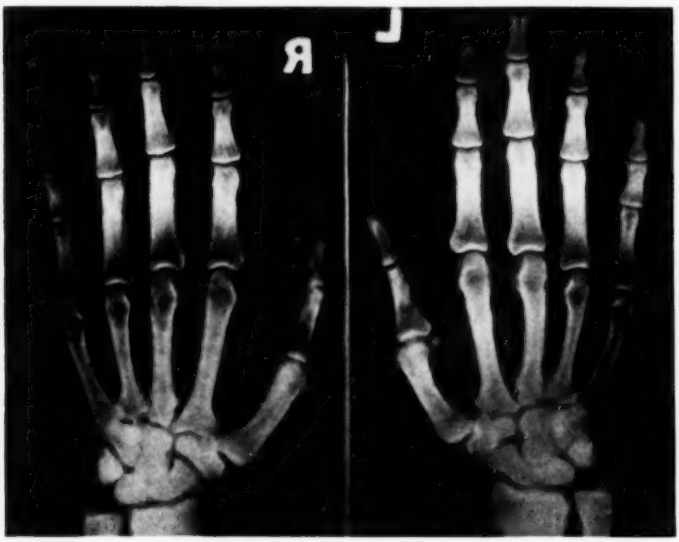

Fig. 3 (Case 2).—Cyst-like lesions in the distal phalanges of both hands, all of which are surrounded by a zone of sclerosis. The escalloped defect on the base of the proximal phalanx of the right thumb probably represents a cyst-like lesion on the surface.

out areas of destruction in the head, neck, or base of the phalanges near the articular margins, with small flakes of bone in the periarticular soft tissues. 5. Boeck's sarcoid. In this disease, small circular or ovoid areas of destruction near the articular ends of the bones without any evidence of bone atrophy or osteoporosis may so closely resemble the lesions of tuberous sclerosis that they cannot be distinguished roentgenographically. In Boeck's sarcoid, however, there is usually coarsening and disintegration of the trabeculae, a change which is very characteristic. 6. Hypertrophic arthritis. Cyst-like changes may occur in the subarticular regions of the bone; however, these are accompanied by hypertrophic changes at the margins, which are characteristic of the disease. Likewise, this condition is usually general-

ized and not limited to one or two joints of the hands or feet. None of these conditions is associated with calcifications within the skull or brain.

Another type of osseous manifestations in the hands and feet is an irregular cortical thickening, usually present in the metacarpal or metatarsal bones, as demonstrated in Case 4.

CASE 4.—K. M., a white woman aged 36, the mother of four children, was an emotionally unstable person, with frequent temper tantrums. As a result, she had great difficulty in properly caring for her children, so that they had to be placed in foster homes. Two of the children had convulsions; however, they could not be brought in for examination. The youngest of the four children died of an injury, at the age of 1½ years.

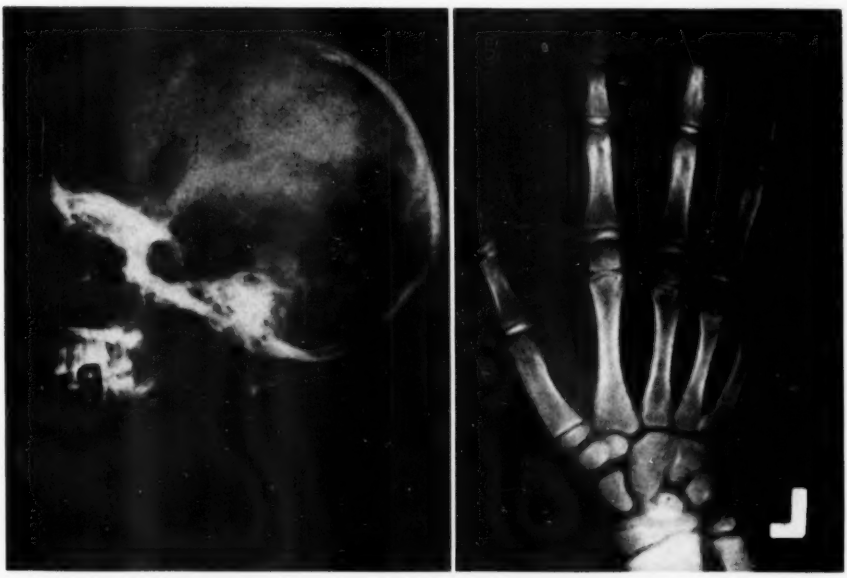

Fig. 4 (Case 3).—*A*, flaky cluster of calcifications within the cranial vault. Thinning of the inner table of the frontal bone is also present. *B*, small "cystic" area in the distal phalanx of the left index finger, the only osseous lesion found in the hands and feet in this case.

The mother herself had had convulsions since infancy; they had been controlled fairly well with phenobarbital. She still had petit mal convulsions, but they were not as severe or as frequent as formerly. She was of low-average intelligence.

Physical examination revealed a fine eruption involving the nose, chin, and both cheeks and shading off to the sides of the face. These lesions of adenoma sebaceum ranged from pinhead to split-pea in size. A nevus was present in the left zygomatic area. The rest of the examination revealed an essentially normal condition.

Roentgenograms of the skull showed several discrete asymmetrical calcifications lying bilaterally within the middle cranial fossa. There was also thickening of the inner table of the parietal bones near the midline (Fig. 5*A*). The roentgenograms of the feet showed irregular thickening of the cortex of the shafts of the second, third, and fourth metatarsal bones bilaterally (Fig. 5*B*). No other osseous lesions were noted in the feet and hands.

These changes in the bone should be differentiated from several conditions: 1. Melorheostosis. In this disease there are deposits of dense bone along the sur-

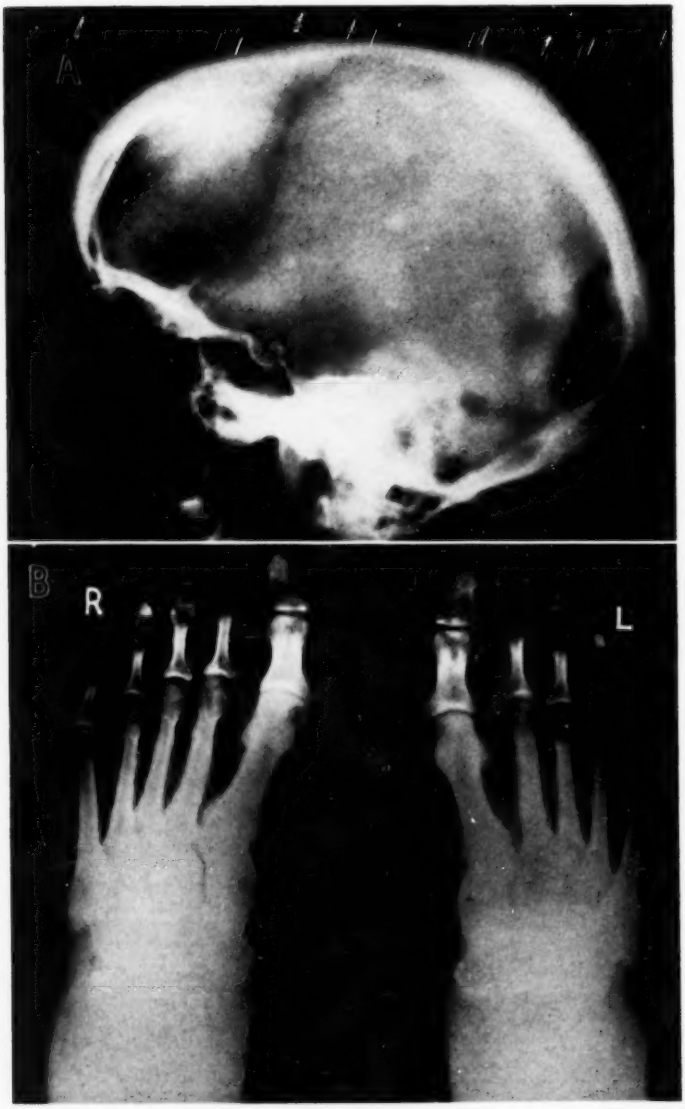

Fig. 5 (Case 4).—*A*, small dense asymmetrical calcifications within the brain. In addition, there is thickening of the parietal bones near the midline. *B*, irregular thickening of the cortex of the second, third, and fourth metatarsal bones of both feet.

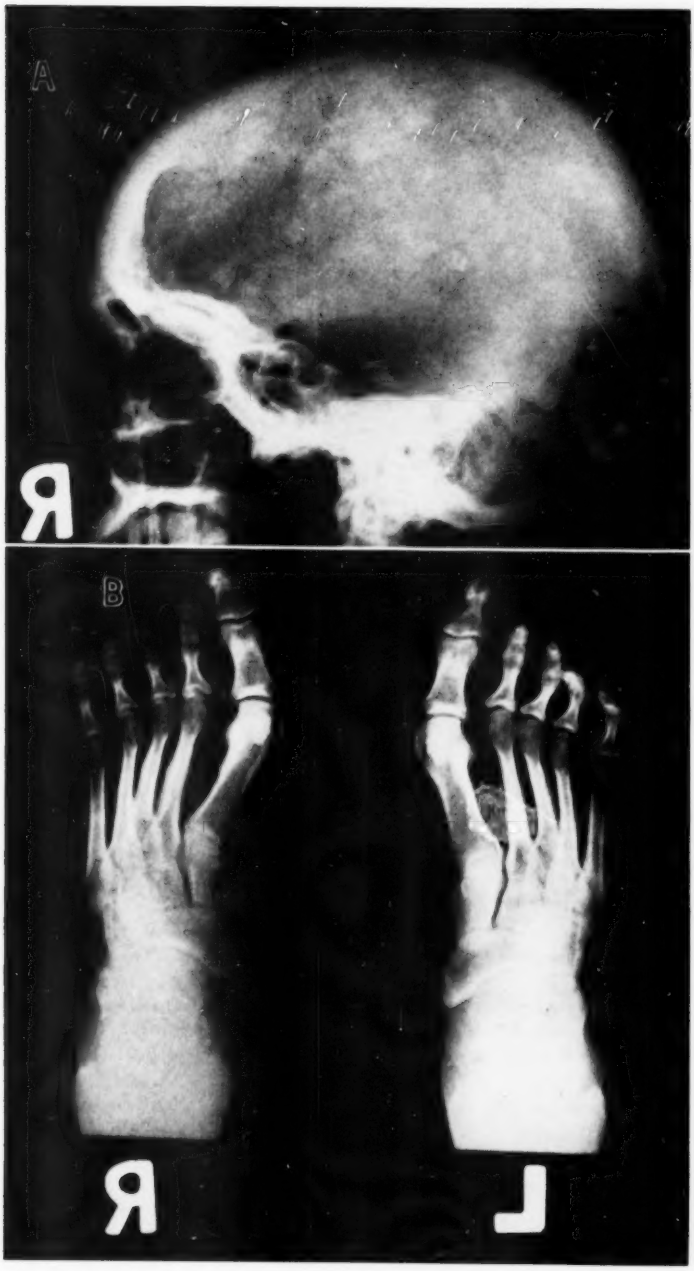

Fig. 6 (Case 5).—*A*, fleecy calcifications scattered throughout the cranial vault and marked thickening of the tables of the skull. *B*, irregular thickening of the cortex of the shafts of the metatarsal bones bilaterally; "cystic" lesions in the distal phalanges of the great toes and the proximal phalanx of the left fourth toe.

face, producing a similar thickening of the shaft. Melorheostosis usually follows the distribution of a nerve and involves more than one bone of an extremity. The cortical thickening often extends to the margin of the joint, indicating that it is not due to periosteal thickening. 2. Periostitis (inflammatory). In this condition there is a thin line of new bone formation, with a dark zone along the shaft showing the normal bone structures beneath. 3. Syphilitic sclerosis. The entire cortical structure is replaced with dense bone, so that the picture resembles very closely the type in Case 4; a destructive area within the center of the area of sclerosis is very characteristic.

A third type of osseus manifestations in the hands and feet may be a combination of the two types represented by the preceding cases. This type is demonstrated in Cases 5, 6, and 7.

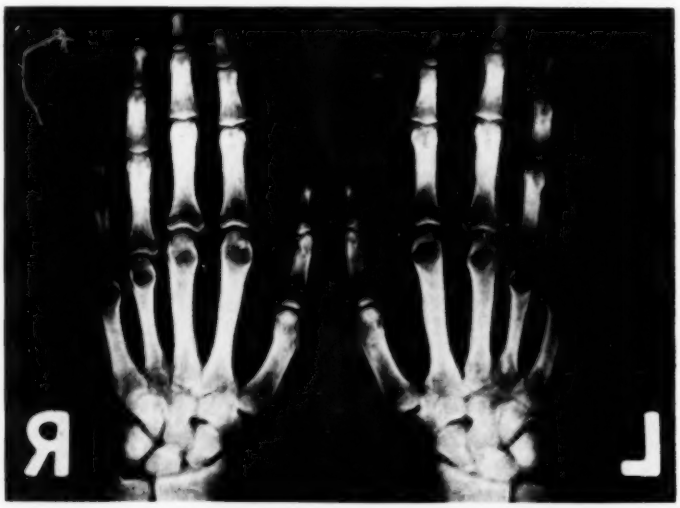

Fig. 7 (Case 5).—Irregular thickening in the proximal phalanges of the middle and ring fingers bilaterally.

Case 5.—M. J., a white woman aged 26, was well nourished and well developed. She had pronounced adenoma sebaceum with a butterfly distribution over her face. The physical condition was otherwise essentially normal. Urinalysis, blood count and serologic tests gave normal results. She had had convulsive seizures since she was 11½ months old. At the time of examination, they were well controlled with diphenylhydantoin and phenobarbital. Her intelligence quotient was 32.

Roentgenograms of the skull showed prominent thickening of the tables of the calvaria, with fleecy calcifications scattered throughout the cranial vault (Fig. 6*A*). Roentgenograms of the feet showed irregular thickening of the cortex of the second, third, and fourth metatarsals bilaterally. There was localized cortical thickening of the first metatarsals bilaterally. A cyst-like formation was present in the distal phalanx of the great toes and the proximal phalanx of the left fourth toe (Fig. 6*B*). Both hands showed irregular thickening of the cortices of the shafts of the proximal phalanges of the middle and ring fingers (Fig. 7).

Case 6.—P. K., a boy aged 11½ years, began having generalized convulsions in early childhood. He was the second of the three siblings of whom M. K. (Case 1) was the oldest. At about 2 years of age there developed a fine papular eruption with a butterfly distribution over

the face. He did not start talking until he was about 4½ years old. He was definitely retarded in all phases of mental development. The intelligence quotient was 51, and he showed definite evidence of brain damage.

On physical examination he appeared well developed and cooperative. He was mentally retarded. The skin showed numerous depigmented areas and a patch, measuring 2 by 2 cm., of "elephant skin" over the lumbar region. He also had a fine papular eruption with a butterfly distribution over the face. The left eye showed a small nodule in the retina resembling a "phacoma," but the disk was normal. The right eye was normal. There was deformity of the middle phalanx of the right middle finger. The physical condition was otherwise essentially normal.

Roentgenograms of the skull showed fleecy areas of calcification within the cranial vault, mostly in the middle cranial fossa on the right. There were several areas of decreased density

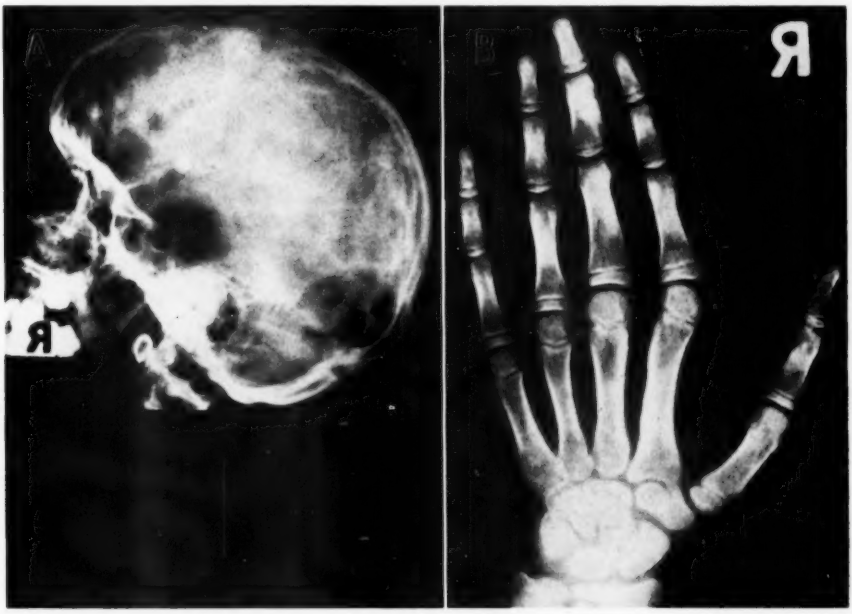

Fig. 8 (Case 6).—*A*, irregular, asymmetrical calcifications in the cranial vault. The convolutional markings are prominent, and there is thinning of the calvaria in the occipital region. *B*, bowing of the second metacarpal bone of the right hand, with thickening of the medial cortex of the shaft. In addition, there is sclerosis, with some fragmentation of the lateral cortex of the shaft of the middle phalanx of the middle finger. (Unfortunately, some of the detail is lost in this photographic print.)

in the occipital region and an increase in the convolutional markings of the cranial vault (Fig. 8*A*).

Roentgenograms of the right hand showed bowing of the second metacarpal bone with thickening of the medial cortex of the shaft. There was also some thickening of the cortex of the adjacent portion of the third metacarpal bone. Similar findings were present in the proximal phalanx of the index and the middle fingers. There was also an area of sclerosis with cyst-like changes or fragmentation along the surface of the shaft of the middle phalanx of the middle finger (Fig. 8*B*).

Case 7.—P. R., a well-nourished white woman aged 19, had right hemiplegia. She walked and ran with a definite limp but was very active. She had no vocabulary but did have a voice. She was completely untrained. Her epileptic seizures were of the petit mal type and were mani-

fested by twitching about the mouth and occasional twitching of the right arm. Her first convulsion had occurred at the age of 10½ months and had been frequent since. When 10 months old, she had postvaccinal encephalitis, at which time the right hemiplagia developed.

The physical condition was essentially normal except for spastic paralysis of the right arm and leg and adenoma sebaceum of the face. The urine, blood, and serologic reactions were normal.

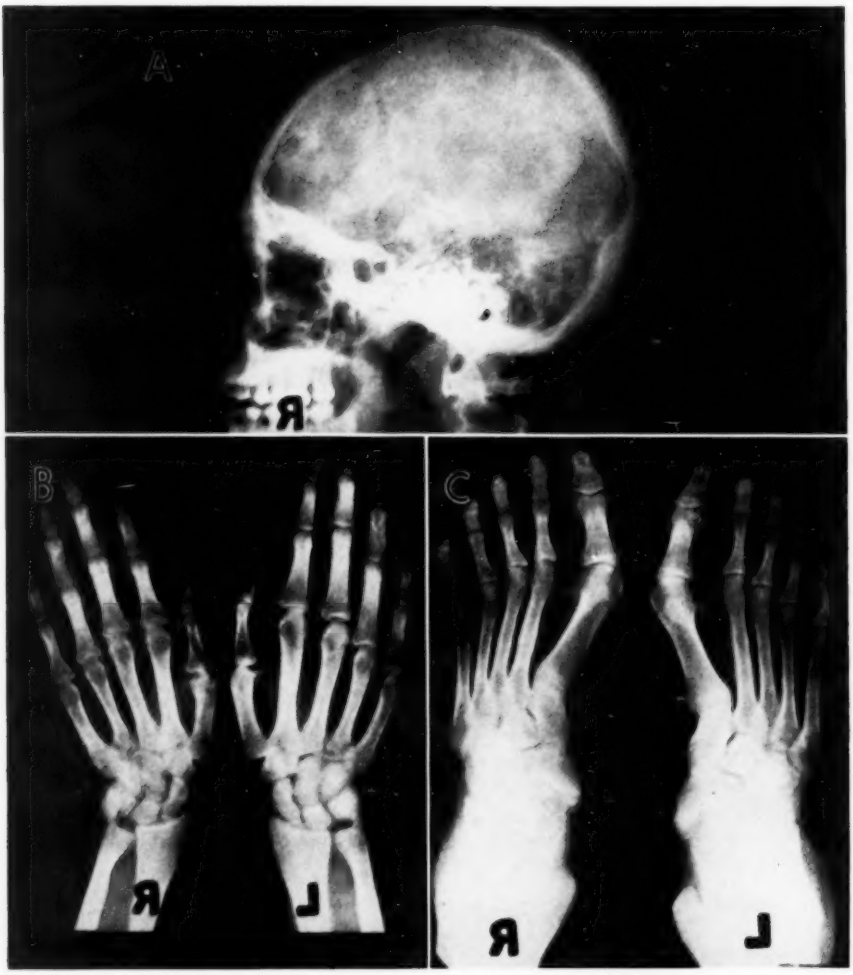

Fig. 9 (Case 7).—*A*, skull of a microcephalic girl, with definite thickening of the tables of the cranial bones. Numerous calcified plaques are scattered throughout the skull. *B*, small cyst-like areas in the distal phalanx of the right middle finger and the middle phalanx of the left ring finger. There also is thinning of the cortex of the middle phalanges of the middle and ring fingers on the right hand, the middle phalanx of the left ring finger, and the middle and proximal phalanges of the left little finger.

C, "cystic" area in the distal phalanges of the great toes and irregular thickening of the cortices of the second, third, and fourth metatarsal bones of both feet.

Right lateral roentgenograms of the skull showed definite thickening of the tabes of the cranial bones. Numerous calcified plaques were scattered throughout the skull (Fig. 9 *A*).

Roentgenograms of the right hand showed a small cyst-like area in the distal portion of the distal phalanx of the middle finger. There also was some thinning of the cortex, suggestive of erosion in the midportion of the middle phalanx of the middle and the ring finger bilaterally and of the phalanges of the left little finger. Another cyst-like area was seen in the middle phalanx of the left ring finger (Fig. 9 *B*). The right foot showed a cyst-like area in the distal portion of the distal phalanx of the great toe. There was also a symmetrical thickening of the cortex of the second and third metatarsal bones. The left foot showed a cyst-like lesion in the distal phalanx of the great toe and a thickening of the cortex of the second metatarsal bone (Fig. 9 *C*).

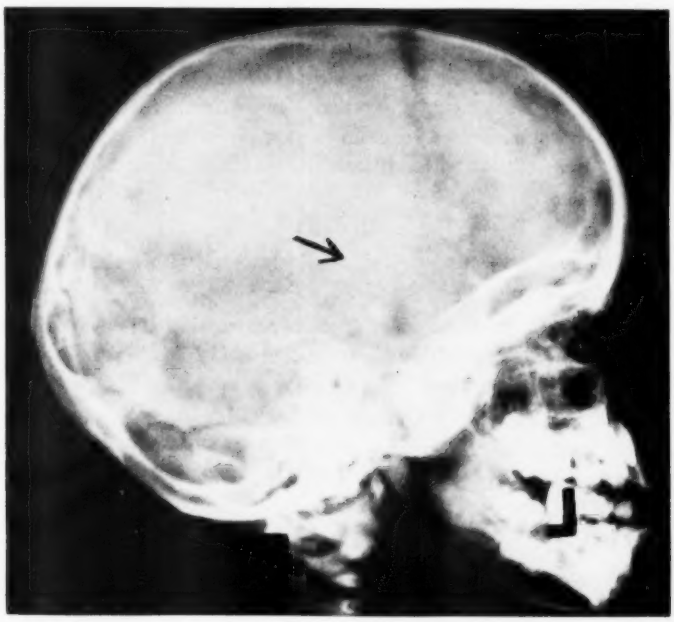

Fig. 10 (Case 8).—Roentgenogram of the skull. The original roentgenogram showed several small faint flaky deposits of calcium in the middle cranial vault which are not readily seen in this reproduction. The arrow points to the area in which they were visualized on the roentgenogram.

Although this series of cases is extremely small, the percentage of osseous changes in the hands and feet corresponds roughly with others that have been reported. In approximately 65% of the cases abnormalities in the hands and feet are demonstrable. If one keeps in mind that this underlying pathologic process is due to a dysplasia of the germinal layers, the dynamics of the osseous changes can be better understood. This dysplasia explains why cyst-like changes in the bone may be present, along with a thickened or fragmented cortex.

In approximately 35% of the cases there may be no osseous manifestations in the hands or feet but calcifications may be present within the skull or brain, as demonstrated in the following case.

Case 8.—S. K., aged 4½ years, the youngest of the three siblings (Cases 1 and 6), had had convulsions since infancy. These manifested themselves first as starting and slight twitching of

the extremities and face. They progressed in severity and frequency but were fairly well controlled for several months with methylethylphenylhydantion (Mesantoin), phenacemide (Phenurone), and glutamic acid. At the time of examination she was receiving diphenylhydantoin (Dilantin) and had an occasional convulsion. She was not as irritable or destructive as she had formerly been.

On examination she appeared well developed and well nourished but retarded. Examination of the eyes, including a funduscopic study, showed a normal condition. The skin was normal. The chest, abdomen, and extremities were normal. The reflexes were hyperactive. An electroencephalogram showed definite changes consistent with a convulsive disorder.

Roentgenograms of the skull showed a few small calcareous deposits within the cranial vault (Fig. 10). Roentgenograms of the hands and feet revealed no evidence of osseous abnormality.

This patient showed beginning areas of calcification at the age of 4½ years. This apparently is the earliest age at which calcifications appear within the skull in this disease. Apley, cited by Kessel,[14] presented a case in which calcifications were not evident at the age of 3 years 9 months. The patient, when reexamined at the age of 5 years 9 months, showed a definite area of calcification. The earliest age at which calcifications appear within the cranial vault can be estimated to be 4 to 4½ years.

COMMENT

There are many conditions producing calcifications within the skull that must be differentiated from tuberous sclerosis.

1. Multiple telangiectasis. Calcium deposits occur within the wall of the vessels and appear as parallel linear calcifications on the surface of the brain. This occurs in a small percentage of the cases.

2. Meningioma. Calcification appears within the tumor in about 10% of cases. The area of calcification may vary from a small plaque to a large amorphous mass. There may be localized hypervascularity with erosion of bone in 25% of the cases. In 35 to 40% of the cases there is hyperostosis of the bone adjacent to the lesion.

3. Sturge-Weber syndrome. In this condition the calcification occurs in the walls of the dilated vessels of the cerebral cortex. The occipital and temporal lobes are the ones usually involved, and they undergo degeneration. Calcium also appears in the outer layers of the cortex of these lobes, frequently producing a large irregular calcification with a gyriform pattern.

4. Calcified subdural hematoma. This lesion may appear as an irregular granular calcified plaque adjcent to the inner table of the skull. Occasionally a smooth line of calcification outlines the margin of the hematoma. There also may be calcifications within this margin.

5. Tuberculoma. A single or several small flecks of calcium surrounded by calcium may appear at the periphery of the lesion. The characteristic finding is an irregular, broken shell of calcification with or without calcification within it. The calcium flecks may coalesce to present a large, massive area of calcification. The calcifications usually are multiple but may be single. Only a small percentage of tuberculomas calcify.

14. Kessel, F. K.: Some Radiological and Neurosurgical Aspects of Tuberous Sclerosis, Acta psychiat. et neurol. **24**:499-522, 1949.

6. Hemangioma of the skull. This condition presents a fairly characteristic picture of spicule formation, with radiation from a center without prominent vascular markings. The lesion is more sharply circumscribed than a meningioma.

7. Cysticercosis. This condition is rare in the United States. The calcification is within the scolex and is surrounded by a calcified cyst wall; it is visible when viewed with a magnifying glass. The calcifications are very small and are scattered throughout the brain.

8. Toxoplasmosis. Calcification occurs in the majority of cases of this disease. The calcifications are small, measuring 1 by 3 mm. in diameter; they are rounded and sharply outlined. They may be unilateral or bilateral and are found in the cortex thalamus, and cerebral ganglia. Occasionally the calcifications may be arranged in curvilinear streaks.

9. Hippel-Lindau disease. The common findings are hemangioblastoma of the cerebellum associated with vascular lesions in the retina. Calcification occurs within the tumor and may appear as a small single fleck or several flecks, which later coalesce. Occasionally a calcium deposit can be seen within the eye.

10. Neoplasms. The calcifications are usually unilateral and single but may be multiple. They may vary from a flaky cluster to a dense homogenous mass.

SUMMARY

The calcifications of the skull and brain found in tuberous sclerosis are multiple and bilateral. They vary in size and shape and may be within the bones of the calvaria or in the brain.

The osseous changes in the hands and feet are of more signficance than was formerly believed. The diagnosis of tuberous sclerosis should always be considered when (1) cyst-like lesions are present in the phalanges; (2) irregular thickening of the cortex of the metatarsal or metacarpal bones is present, or (3) irregular thickening of the cortex of any of the bones of the hands or feet associated with fragmentation or cyst-like changes is present. When these findings present themselves with calcifications within the skull, the diagnosis can be clearly established. The percentage of cases in which both these changes are present can be estimated to be between 60 and 65%.

Dr. A. A. Hines, superintendent of the St. Louis Training Schools, made available the records of the patients.

LANGUAGE BEHAVIOR IN PSYCHONEUROTIC PATIENTS

MARIA LORENZ, M.D.
AND
STANLEY COBB, M.D.
BOSTON

THE FORMAL linguistic categories grammar and syntax seem at first sight remote from psychological significance. Psychiatric literature contains relatively few studies of this aspect of language. The reason lies partly in the fact that psychiatrists are especially schooled to look beyond and through words to the things for which they stand. Yet there has long been an awareness that this formal dimension of language, apart from content, is capable of giving certain kinds of information about habits of thought and feeling.

Comparative language studies lend support to this view. In peoples in whom the mental set differs from ours, grammatical categories of a different order dominate the speech pattern. In the Mayan tongue [1] the leading idea is the purposiveness and use of things, in contrast to our own emphasis upon a relation between things. Our language mirrors this "mental set" in the primacy of subject-predicate relationships, whereas the Mayan substitutes occurrences for things and hence uses a category of grammar for which our language has no exact equivalent. The Kaingang Indians of Brazil [2] made sentences with neither subject nor object so that disagreeable things could be talked about without mentioning what or which.

Observations such as these suggest that the functional structure of language, grammar and syntax, determines the form in which mental content is presented and may be assumed to reflect mental habits of direction and organization. If this hypothesis is correct, it may be of relevance to psychiatric investigation in introducing a level of inquiry susceptible to quantitative methods of study.

It would make it possible to investigate the language of groups of psychoses and the neuroses for objective evidence in trends of thinking or mental set that differ significantly from those we choose to call normal. In a preliminary study [3] on language behavior in manic reaction types, statistically significant differences in the pattern of word distribution were found which seemed to be open to correlation with psychological traits. In the present study this method of inquiry is extended to a group of psychoneurotic patients.

This is the fourth in a series of papers on language.

From the Massachusetts General Hospital Branch of the Hall-Mercer Hospital, the Massachusetts General Hospital, and the Department of Neurology and Psychiatry of the Harvard Medical School.

1. Gates, W. E.: A Grammar of Maya, Baltimore, The Maya Society, 1938.

2. Jules, H.: The Linguistic Expression of Emotion, Am. Anthropologist **38**:250-256, 1936.

3. Lorenz, M., and Cobb, S.: Language Behavior in Manic Patients, A. M. A. Arch. Neurol. & Psychiat. **67**:763-770, 1952.

MATERIAL, METHOD, AND OBSERVATIONS

Empirical studies of language characteristics of psychoneurotic subjects are few. Obviously, in such a widely heterogeneous group one would have no reason for assuming that characteristic patterns of speaking would hold. But within this broad classification clinical observations point to certain uniformities that make selection of this group justifiable. Anxiety, either bound or free, an intense and continuous self-awareness and self-preoccupation, and a tendency to remain fixed within the area of their conflict are noted. It is possible to differentiate roughly broad character types with their own characteristic defense mechanisms and comparable dynamics in the development of symptoms. When we speak of "hysterical char-

TABLE 1.—*Individual 1,000-Word Samplings of "Normal," "Neurotic$_s$" and "Neurotic$_t$" Speech,* Analyzed for Distribution of Words as Parts of Speech†*

Individual 1,000-Word Samplings	Substantives			Adjectives			Adverbs			Main Verbs			Auxiliary Verbs		
	N	N_s	N_t	N	N_s	N_t	N	N_s	N_t	N	N_s	N_t	N	N_s	N_t
1	20.5	14.4	15.1	15.5	14.5	15.7	15.7	18.0	19.3	15.1	20.4	20.8	4.9	7.4	10.3
2	18.9	13.8	14.2	14.7	12.9	13.9	15.5	17.8	17.8	14.4	20.3	18.5	4.6	7.1	8.4
3	18.6	12.5	13.5	13.6	12.8	12.8	15.3	17.2	16.9	13.7	19.1	17.5	4.6	6.9	8.1
4	17.4	11.6	12.7	12.7	11.7	12.6	13.0	15.0	14.7	13.3	17.8	17.2	4.3	6.8	7.4
5	16.9	11.4	11.2	12.3	11.4	10.6	12.3	14.8	14.3	13.2	16.5	16.9	3.9	6.7	6.4
6	16.3	10.6	10.7	11.5	10.1	10.6	11.4	14.1	14.0	12.6	15.7	16.8	3.5	6.4	6.3
7	15.8	10.3	10.1	11.4	9.8	10.4	11.3	12.8	12.9	12.6	15.7	15.8	3.4	6.3	5.7
8	15.7	9.4	9.3	10.5	8.4	10.0	11.3	12.6	12.7	12.3	15.6	15.6	3.4	6.1	5.6
9	14.1	8.2	8.9	10.3	8.1	9.2	10.2	12.0	12.6	12.0	15.3	15.3	3.3	5.9	5.5
10	12.9	8.1	8.6	9.1	6.7	6.6	9.1	7.9	12.4	11.0	11.5	14.9	2.5	5.6	4.7

Individual 1,000-Word Samplings	Pronouns			Prepositions			Conjunctions			Articles			Interjections		
	N	N_s	N_t	N	N_s	N_t	N	N_s	N_t	N	N_s	N_t	N	N_s	N_t
1	17.6	26.2	24.4	12.1	7.7	9.4	11.9	9.7	8.4	8.2	6.5	8.6	7.0	3.3	2.4
2	16.9	26.0	22.2	11.7	7.4	8.2	11.5	9.1	8.2	7.4	5.1	7.8	5.8	3.1	1.4
3	15.3	25.6	20.2	11.1	7.1	8.1	10.4	7.9	7.5	7.2	4.8	7.0	3.1	2.6	1.2
4	14.5	24.0	20.0	11.1	6.6	7.5	10.3	7.7	7.2	7.2	4.8	6.5	2.5	0.9	0.7
5	14.2	22.9	20.0	10.7	6.2	7.1	9.5	7.3	7.0	6.2	4.7	5.3	1.8	0.4	0.7
6	14.1	20.4	17.6	10.3	6.2	7.0	8.5	7.0	4.8	6.1	4.7	5.2	1.4	0.3	0.6
7	13.9	20.3	15.4	9.7	5.6	6.9	8.2	5.6	4.7	5.5	4.3	5.2	0.8	0.3	0.5
8	10.9	18.6	15.4	9.6	5.5	6.2	7.0	5.1	4.6	5.5	4.0	4.9	0.6	0.3	0.4
9	10.7	18.2	15.3	8.8	5.0	5.1	6.0	4.9	4.2	5.2	3.6	4.6	0.4	0	0.4
10	10.5	17.9	13.6	8.6	4.3	5.1	5.8	4.2	3.8	5.1	3.4	2.7	0.4	0	0.3

* N indicates normal-spontaneous; N_s, neurotic-spontaneous, and N_t, neurotic-thematic speech.
† Values arranged in order of decreasing magnitude and expressed as percentages.

acter" as opposed to the "obsessive-compulsive" character, or the "oral" as opposed to the "anal" character, we are aware that these are convenient abstractions and do not exist in pure form. Nevertheless, certain patients can approximately be grouped in an arbitrary way and tend to be more similar to each other in psychological make-up than to another group. "Hysteria" as a classification carries with it the implication of a tendency to repression and conversion as mechanisms of defense, a strong tendency to self-expression, often taking a dramatic or histrionic form, a feeling-toned and emotional, rather than an intellectual, evaluating kind of relationship to the external world. Suggestibility is marked.

For this study 10 patients with a clinical diagnosis of "psychoneurosis, hysteria," and fulfilling the characteristics briefly sketched above were selected. All the patients were severely handicapped or incapacitated by their neurosis. The mean educational level was high-school education, one patient falling above and one below this mean. In the group of "normal" persons used for comparison the level of formal education was somewhat higher. So far as individuals

were concerned, the rating in word-frequency studies and in pattern of grammatical distribution did not appear to correlate specifically with intellectual sophistication and level of culture. This was reflected in the qualitative content rather than in the quantitative pattern.

In order to determine the effect of a change in topic and of motivation in the stream of speech, we compared samplings of "spontaneous" speech of the "neurotic" subjects with samplings obtained when the same subjects were presented with two TAT (Thmatic Appreciation test) cards to describe and discuss. One of these cards presented a quiet, serene view of nature; the other depicted a vivid, emotional episode involving two people.

"Spontaneous" speech samples were arbitrarily selected from the content of interviews in which the patient felt at ease and talked of some preoccupying aspect of himself. This consisted

TABLE 2.—*Recurrence of Words as Parts of Speech in Ten 1,000-Word Samplings of "Normal," "Neurotic-Spontaneous," and "Neurotic-Thematic" Speech, Expressed in Percentages*

Grammatical Divisions	"Normal"	P *	"Neurotics"	"Neurotics"	P *
Substantives	16.7	> 0.01 †	11.0	11.4	0.6-0.5
Adjectives	12.2	> 0.01 †	11.6	11.2	0.5-0.4
Adverbs	12.5	0.1-0.05	14.2	14.8	0.6-0.5
Main verbs	13.0	> 0.01 †	16.8	16.9	0.9-0.8
Auxiliary verbs	3.8	> 0.01 †	6.5	6.8	0.5-0.4
Pronouns	13.8	> 0.01 †	21.9	18.4	> 0.01 †
Prepositions	10.4	> 0.01 †	6.2	7.1	0.06-0.02 †
Conjunctions	8.9	> 0.01 †	6.9	6.1	0.4-0.3
Articles	6.4	> 0.01 †	4.6	5.8	0.1-0.05
Interjections	2.4	....	1.1	0.9	0.7-0.6
Conceptual-articulatory ratio	1.19	0.1-0.05	1.12	1.20	0.02 †
Verb-adjective quotient	1.07	> 0.01 †	1.70	1.61	0.02 †

* *P* denotes probability value, as determined by the *t* test, and represents the result of comparison of "Normal" with "Neurotics" (neurotic spontaneous") and of "Neurotics" ("neurotic thematic") with "Neurotics."

TABLE 3.—*Recurrence of Words as Parts of Speech in Ten 1,000-Word Samplings of "Neurotic," "Normal," and "Manic" Speech, Expressed in Percentages*

Grammatical Divisions	"Neurotic"	P*	"Normal"	"Manic"	P*
Substantives	11.0	> 0.01†	16.7	14.9	0.1-0.05
Adjectives	10.6	> 0.01†	12.2	9.6	> 0.02-0.01
Adverbs	14.2	0.1-0.05	12.5	11.7	0.5-0.4
Main verbs	16.8	> 0.01†	13.0	16.1	> 0.01†
Auxiliary verbs	6.5	> 0.01†	3.8	6.2	> 0.01†
Pronouns	21.9	> 0.01†	13.8	18.2	> 0.01†
Prepositions	6.2	> 0.01†	10.4	8.3	> 0.01†
Conjunctions	6.9	> 0.01†	8.9	7.5	0.2-0.1
Articles	4.6	> 0.01†	6.4	5.9	0.3-0.2
Interjections	1.1	0.1-0.05	2.4	1.7	0.5-0.4
Conceptual-articulatory ratio	1.12	0.1-0.05	1.19	1.09	0.3-0.2
Verb-adjective quotient	1.70	> 0.01†	1.07	1.68	> 0.01†

* *P* denotes probability value, as determined by the *t* test, and represents the comparison of "Neurotic" with "Normal" and of "Manic" with "Normal."
† Statistically significant.

in every instance of a mixture of material having to do with recent and remote experiences, his symptoms, and reflections upon these topics. The content of the "normal" samplings (the same as those previously used for comparison with "manic" speech samples) consisted of recent and remote life experiences, comments, and reflections thereupon.

Samplings of 1,000 consecutive words were taken at random from a 15-minute recording of spontaneous flow of speech of each of the 20 subjects. Samplings of the responses to the TAT cards were taken so that each of the 10 samples represents the total number of words used by each patient to exhaust his response to the stimulus. These samples averaged 525 words per patient. Analysis showed that the size of the sample influenced the results if fewer than 300 words were used.

In terms of grammatical construction, uniformity in analysis was maintained by having the same person qualify the words as parts of speech. The *t* test,[4] as an application of the critical ratio to small samples, was applied wherever feasible, and the results which have statistical significance on the basis of this test are starred. This test takes into account the increasing unsatisfactoriness of representative measurements as the size of the sample decreases.

The production and use of language by different subjects, and even by the same subject at different times, are subject to so many variables that the concept of an adequate control is untenable. However, landmarks can be established whereby one roughly approximates trends in the same or different directions. For this reason, comparison is made with the language pattern of psychotic patients, as well as with that of normal persons. Interpretations of the differences observed in the language patterns of different groups, despite demonstration of statistical significance, are to be viewed as broad indications of directions and trends, not as specific values.

RESULTS

Language Patterns.—Table 1 represents individual 1,000-word samplings of "normal," "neurotic-spontaneous," and "neurotic-thematic" speech, analyzed for distribution of words as parts of speech. Values are arranged in order of decreasing magnitude and expressed as percentages. The use of words as parts of speech falls within a fairly uniform distribution range for the samples of the series.

TABLE 4.—*Word-Frequency Distribution in "Neurotic," "Normal," and "Manic" Speech Based on Ten 1,000-Word Samplings*

	"Neurotic"	*P* *	"Normal"	"Manic"	*P* *
Ten most frequently used words	I, and, the, to, a, of, **it**, that, **is**, you	.....	I, and, the, to, a, of, in, that, my, was	I, and, the, to, a, of, in, that, **it**, was	.....
Recurrence of most frequently used word ("I") per 1,000 words	94	0.05-0.02 †	66	69	>0.05
No. of words used once per 1,000 words	154	>0.01 †	200	183	>0.05
No. of different words per 1,000 words	289	>0.01 †	341	315	0.05-0.02 †
No. of different words having rank-frequency distribution of 1:10 in 10 samples	25 48% conceptual words		31 48% conceptual words	42 57% conceptual words	.....

* *P* denotes probability value, as determined by the *t* test, and represents the result of comparison of "Neurotic" with "Normal" and of "Manic" with "Normal."
† Statistically significant.

Table 2 shows the findings in Table 1 analyzed statistically.

Interpretation: The language pattern of a given group retains its identity despite change in topic and focus.

Table 3 represents a comparison of the language pattern of three different populations: "neurotic," "manic," and "normal" persons.

Interpretation: The language pattern of "neurotic" subjects shows a significant relative increase in the use of verbs and pronouns and a significant relative decrease in the use of substantives, adjectives, prepositions, conjunctions, and articles. The language pattern of "manic" patients shows changes in a similar direction, e. g., a significant relative increase in the use of verbs and pronouns and a significant relative decrease in the use of adjectives and prepositions. The verb-adjective quotient for both the "neurotic" and the "manic" group is significantly higher than that for the "normal" group.

4. Fisher, R. H.: Statistical Methods for Research Workers, Ed. 10, Edinburgh, Oliver & Boyd, Ltd., 1946.

The language pattern of "neurotic" subjects appears to be more strongly differentiated from the pattern of "normal" persons than does the "manic" pattern. This finding is open to two interpretations, either (1) that the use of language by "neurotic" patients is more homogeneous within the group, or (2) that the selection of the group of "neurotic" patients has been more homogeneous.

Word-Frequency Studies.—Table 4 represents a comparison of word-frequency distribution in "neurotic," "normal," and "manic" persons.

1. For the 10 most frequently used words, "neurotic" language patterns differ from "normal" patterns in the use of the pronouns "it" and "you" and the substitution of the verb "is" for "was."

Interpretation: Copulative verbs have two functions: (1) that common to all verbs, of establishing a relationship, and (2) that of making an assertion. A preferential use of the present tense would seem to indicate that the ideation content, or subject matter, lies within the realm of immediate experience and that at the time of speaking the speaker was primarily oriented in the immediate situation or experience.

Use of the pronoun "you" would seem to indicate that the auditor is definitely drawn into the situation or experience, or that there is an awareness of the auditor's reaction. An exception would be if "you" were used primarily as part of a speech stereotype, such as "you know" or "you see" (a feature common to the manic speech pattern).

Use of the pronoun "it" underlines either (1) a recurrence of the same subject matter, originally defined by a nominal term, or (2) vagueness in particularizing.

2. The incidence of the pronoun "I" is significantly higher in "neurotic" language patterns than in "normal" and "manic" language patterns.

Interpretation: The "neurotic" subject is either less flexible in shifting from the subjective point of view or less given to disguising or dissimulating this attitude than the other groups.

3. In the "neurotic" language pattern, significantly fewer different words occur per thousand, and the number of words used once per thousand is less than in the "normal" pattern.

Interpretation: If, from the standpoint of communication, language is regarded as a code in which words are the signs, the number of different signs used and the frequency of the recurrence (within a given sample) give a quantitative estimate of the diversity and flexibility in the use of the code. The quantitative measurements here point to a less diverse and flexible use of the instrument of communication by "neurotic" than by "normal" subjects. The same finding held for the use of language by a selected group of "manic" patients.

4. In the "neurotic" language pattern fewer different words fall within the highest frequency range than in the "normal" pattern. This is in sharp contrast to the "manic" language pattern, in which the trend is in the opposite direction.

Interpretation: The number of different words occurring within the high range of frequency distribution in 10 language samples of one group as compared with that in another group represents a measure of the uniformity or similarity of the samples

within each group. It may then be said that the subjects within the "neurotic" group are more homogeneous in their use of language than subjects in the "normal" group, and much more so than subjects in the "manic" group.

5. The "neurotic" and "normal" language patterns are alike in the manner of conceptual words introduced into the highest range of word frequency. In the "manic" pattern a higher per cent of conceptual words is found.

Interpretation: Conceptual words are more differentiated and personal, whereas the articulatory words represent the common currency of language. The observation points to more differentiation and variability in individual use of language within one group (manic) than within the other. It is of interest to speculate whether another psychotic group, such as the schizophrenic, would show this variability to an even greater degree.

REVIEW OF LITERATURE

Two independent directions of investigation contribute to the formulation of the problem and the analysis of the findings which are under consideration in this study. One area is concerned primarily with language in its theoretical aspects, psychological implications, and methodology. A review of the relation of language concepts to psychiatry has been previously attempted by one of us (M. L.).[5] Those points of view particularly relevant to the present discussion are noted below. A second area is concerned more specifically with the psychopathology of the neurosis so far as this lies revealed in language characteristics.

Divergent approaches to language from a speculative point of view are illustrated by Langer's[6] term of "transparency" of language (to indicate that words have no value except as symbols and signs) and the behavioristic approach, exemplified by de Laguna,[7] Skinner[8] and others, who view language as an independent feature of the environment to which the individual adapts himself and which he modifies and shapes for his own purposes. The independent status of language, particularly its statistical structure, and its role as a medium for communication have been well documented by studies by Shannon and Weaver,[9] Bavelas,[10] and Zipf.[11] The stress here is on the view that language is a code, governed by discernible laws within limits predictable in its use. Language has a pattern of its own, a pattern which can be shifted within limits by the user. Shannon and Weaver[9] point out that the redundancy of English is about 50%, "so that half of the letters or words we

5. Lorenz, M.: Language Concepts as Related to Psychiatry, Quart. Rev. Psychiat. & Neurol. **7**:123-138, 1952.

6. Langer, S. K.: Philosophy in a New Key: A Study in the Symbolism of Reason, Rite, and Art, Ed. 2, Cambridge, Mass., Harvard University Press, 1951.

7. de Laguna, G.: Speech: Its Function and Development, New Haven, Conn., Yale University Press, 1927.

8. Skinner, B. F.: Verbal Behavior, Cambridge, Mass., Harvard University Press, 1948.

9. Shannon, C. E., and Weaver, W.: The Mathematical Theory of Communication, Urbana, Ill., University of Illinois Press, 1949.

10. Bavelas, A.: Communication Patterns in Problem-Solving Groups in Cybernetics: Transactions of the 8th Conference, New York, Josiah Macy Jr., Foundation, 1952.

11. Zipf, G. K.: (*a*) Relative Frequency, Abreviation and Semantic Change, in Selected Studies of the Principle of Relative Frequency in Language, Cambridge, Mass., Harvard University Press, 1932; (*b*) The Repetition of Words, Time-Perspective, and Semantic Balance, J. Gen. Psychol. **32**:127-148, 1945.

choose in writing or speaking are under our free choice, and about half (although ordinarily we are not aware of it) are really controlled by the statistical structure of languages." This would seem to have immediate bearing upon Zipf's [12] division of words into conceptual and articulatory. It seems plausible to suspect that the "determined" versus the "free-choice" words are closely related to words carrying meaning (conceptual) and words empty of content but establishing relationships (articulatory). Zipf makes a beginning in correlating empirical data of frequency distribution of words with interpretation in terms of dynamics. He has developed some rather involved speculations with regard to time perspective and semantic balance. However, his point of view is expressed clearly.[11b]: "Distributions may be quite instructive in studying the personality for they may reflect the conscious or unconscious struggles of the personality in altering the tools and objectives of his life." Whitehorn and Zipf,[13] Baker,[14] and Bonsfield and Barclay [15] have applied some principles of the statistical consistency of language empirically. Their studies demonstrate practical possibilities in the application of formal linguistic theories to psychological investigation.

Rowland [16] makes a significant contribution to knowledge of the psychological experiences connected with different parts of speech. Her thesis is that all words, even when they have no specific reference to an object, raise an inner state of expectancy. For example, she notes that adjectives have affective coloring and give a subjective reaction. By contrast, adverbs are less intimate and express an apparent quality or appearance. The movement is away from the subjective to a more objective frame of mind. With respect to nouns, she notes that when images are ignored or, for some reason, are few, the vocabulary is impoverished of concrete nouns. Gardiner [17] and Sheffield [18] make additional contributions in this area. The implication is that the grammatical construction in which a thought is formulated is psychologically related to the mental attitude of the speaker.

Bavelas [10] suggests that the linguistic structure developed in languages of different groups may have structured the fundamental concepts of their users. Jules [2] and Gates [1] develop and illustrate the same point of view, leaning perhaps more to the interpretation that linguistic habits reflect the fundamental concepts of the users. Bühler [19] feels that the functions of demonstration and presentation in various modalities belong as much to language as do its functions of abstracting and conceptualizing. Sheffield [18] indicates that grammar and syntax give "direction"

12. Zipf, G. K.: The Psycho-Biology of Language, Boston, Houghton Mifflin Company, 1935.

13. Whitehorn, J. C., and Zipf, G. K.: Schizophrenic Language, Arch. Neurol. & Psychiat. **49**:831-851, 1943.

14. Baker, S. J.: A Linguistic Law of Constancy, J. Gen. Psychol. **43**:47-62, 1950; A Linguistic Law of Constancy: II, ibid. **44**:113-120, 1951.

15. Bonsfield, W. A., and Barclay, W. D.: Application of Zipf's Analysis of Language to Sequences of Restricted Associative Responses, J. Gen. Psychol. **44**:253-260, 1951.

16. Rowland, E. H.: The Psychological Experiences Connected with Different Parts of Speech, Psychol. Rev., Monogr. Supp. **8**:1-42, 1907.

17. Gardiner, A. H.: The Theory of Speech and Language, Oxford, England, Clarendon Press, 1932.

18. Sheffield, A. D.: Grammar and Thinking, New York, G. P. Putnam's Sons, 1912.

19. Bühler, K.: Sprachtheorie: Die Darstellungsfunktion der Sprache, Jena, Gustav Fischer, 1934.

to the ideational content. The implication of all these theories appears to be that the form of language, as it becomes apparent in grammar and syntax and statistical properties, has a definite relation to organization, direction, and shaping of content material. In other words, the form of language, no less than its content, is psychologically determined.

An approach to language from a behaviorist point of view, as represented by Skinner, also ignores symbolization and meaning and focuses on observable effect and response. Skinner analyzes certain linguistic categories that imply intentions or purposiveness in language behavior. For example, "autoclitics," such as "I say," "I believe," "I suppose," suggest behavior leaning upon itself. Words introducing clauses, e. g., "if," "that," "as," "therefore," are attributed to the speaker's intentions—propositional attitudes. Herman [20] describes the hearer side of typical language behavior segments. Skinner [8] and Carroll [21] both point out that verbal behavior has as yet not been adequately studied or integrated with systematic psychiatric theory. Lashley [22] takes a step in this direction in his discussion of language as an example serial order in behavior. In this paper, in an all-too-short digression, the author gives a behavioristic description, in terms of cerebral mechanisms, to slips of the tongue. As he implies, a description on this level does "not need to accept theories of censorship and suppression." Nor, one may add, does it invalidate them. The two are descriptions of a different order of the same phenomena, and both approaches are potentially useful and valuable.

From the standpoint of method, Johnson [23] has contributed a systematic outline of the practical devices by which language behavior can be studied. Of special value is his type-token ratio, which he interprets as a measure of vocabulary flexibility. Two of his associates, Fairbanks [24] and Mann,[25] have shown the applicability of these methods to the study of group differences in "normal" and in "psychotic" subjects.

Although there is a growing awareness of the psychological implications of the neurotic patient's choice of words and manner of speaking, such studies are primarily dynamically oriented and depend upon interpretation of the content of language rather than on the more objective examination of form and structure. An emphasis toward the latter approach, however, is found in the work of Balken and Masserman,[26] Sanford,[27] Newman,[28] and Glauber.[29] These workers indicate that character structure and speech pattern are closely related.

20. Herman, D. T.: Linguistic Behaviors, J. Gen. Psychol. **44**:199-213, 1951.

21. Carroll, J. B.: The Analysis of Verbal Behavior, Psychol. Rev. **51**:102-119, 1944.

22. Lashley, K. S.: The Problem of Serial Order in Behavior, in Cerebral Mechanisms in Behavior: The Hixon Symposium, edited by L. H. Jeffress, New York, John Wiley & Sons, Inc., 1951.

23. Johnson, W.: Studies in Language Behavior, Psychol. Monogr. **56**:1-15, 1944.

24. Fairbanks, H.: The Quantitative Differentiation of Spoken Language, Psychol. Monogr. **56**:19-38, 1944.

25. Mann, M. B.: The Quantitive Differentiation of Samples of Written Language, Psychol. Monogr. **56**:41-74, 1944.

26. Balken, E. R., and Masserman, J.: The Language of Phantasy, J. Psychol. **10**:75-86, 1940.

27. Sanford, F. H.: Speech and Personality, Character and Personality **10**:169, 1941.

28. Newman, S. S.: Personal Symbolism in Language Patterns, Psychiatry **2**:177-184, 1937.

29. Glauber, P.: Speech Characteristics of Psychoneurotic Patients, J. Speech & Hearing Disorders **9**:18-30, 1944.

COMMENT

An analysis of the findings in this study leads to the following tentative description of pattern and characteristics in the language of 10 patients with an illness diagnosed as "psychoneurosis, hysteria":

Word-frequency studies indicate that the use of language as a code for communication is less flexible than that of "normal" subjects. A preference is given to the use of pronouns and verbs, and relatively less emphasis to substantives, adjectives, and some of the articulatory words. The personal pronoun "I" occurs with significantly higher frequency than in the pattern of the other groups. The second and third person pronouns "you" and "it" appear within the range of the 10 most frequently used words. In the use of verbs the present tense predominates. The verb-adjective quotient, considered by Balken and Masserman as a measurement of anxiety, is found to be high.

The constriction in the spontaneous use of language would seem to document the clinical observation of a narrowing of interests and preoccupation with a specific constellation of mental content. This also holds true for a group of "manic" patients previously studied. The "neurotic" patients as a group are more distinctly differentiated in language pattern from a "normal" group than are "manic" patients. It does not follow that a pattern more sharply differentiated within the areas studied is more "abnormal." The clinical "abnormality" of manic speech, as has previously been indicated,[3] lies on many planes; the least affected are the automatic and formal linguistic characteristics of speech. It seems likely that the selection of "neurotic" speech patterns represents a more homogenous sampling than did the selection of "manic" speech patterns.

It is of interest that in these groups of "neurotic" and "normal" subjects the conceptual-articulatory word ratio of the most frequently used words parallels so closely the 50-50 distribution[9] of consciously selected and automatically determined words that comprise the statistical structure of language. "Neurotic" patients follow a pattern not significantly different from the normal in the content and distribution of conceptual words. "Manic" patients, however, include a somewhat higher content of conceptual ("chosen") words in the most frequently used words, although the total number of conceptual words used is not statistically different from that of the "normal" group.

When words are broken down into functional grammatical units, quite distinct patterns hold for the given groups. An evaluation of this finding is tentative and is presented as an interpretation.

Substantives are the key words, or carrier words, in our language structure. The pattern of language becomes impoverished of substantives under two conditions. So far as the nominal terms become changed to pronouns, the number of substantives, or "name words," become less. This happens obviously when the interest is more narrowly focused and "it" or "that" can conveniently be substituted for the recurrent referent. This does not necessarily denote an impoverishment of ideas, since an indefinite number of variations may be given to a single topic that is referred to by the pronoun. It seems to tell us something, however, about the movement or direction of ideas. A second condition under which substantives decrease is when the sentences become longer and more elaborate in description or qualification, so that fewer sentence units are included in a given sampling. Both

conditions, however, imply the same factor, namely, that there are less flow and direction of the stream of consciousness away from a central idea or theme. This apparently holds true for the "neurotic" group, as it did for the "manic" group.

The high frequency of use of the pronoun "I" also suggests two possibilities—either "I" becomes the subject about which assertions are made, or "I" assumes prominence as a consistently used pointer that gives an egocentric value to the idea expressed. Phrases such as "I am aware of," "I think," "I believe," or "I suppose" may be colorless stereotypies in a given subject (in such examples one or few of these phrases are habitually used), or their use may be dynamically alive and flexible, with many variations of the particular manner in which "I" is related to the statement in which it is involved. In either case, however, a preponderance of the use of "I" establishes strong egocentric emphasis in communication. The speaker appears, consciously or unconsciously, to impress his own characteristics or point of view.

A diminution of articulatory words (prepositions, conjunctions, and articles) would suggest a tenser, more telegraphic style. From the impression given by the verbatim records, however, this is not actually the case. A more likely interpretation is that in a given sample in which certain grammatical elements make up the bulk of the sample, the decrease of others is of relative, rather than absolute, value. More significance is attached to the decrease in conceptual words (substantives and adjectives), since they presumably might be expected to be less affected by the statistical structure of the language and more by the needs and intent of the speaker. The decrease of substantives and subjective qualifications seems to imply less attentiveness and preoccupation in qualifying and differentiating the limited number of topics discussed. The emphasis appears to be on action and movement and on assertion (functions of verbs), qualities that suggest expressiveness and outward projection in mental attitude.

In terms, then, of expressive behavior, the "neurotic" and "manic" speech patterns have something in common. But, apparently, the "neurotic" pattern also takes into account the hearer side of verbal behavior. "You" falls into the high-frequency range of use. Its use suggests an awareness of the listener and a specific direction or intent toward him. "You" could also be used as a vague characterization or generality; i. e., "You never know if." (With these patients, however, "you" was used directly and specifically as an appeal to the listener.)

Time orientation as reflected in the tense of verbs has many facets related to the content of speech. Use of the verb "is" suggests at least orientation in the present. Its use also generally implies that a judgment or assertion is made. The language of "neurotics," therefore, might be considered as more oriented to the present and more assertive than that of the "normals."

An interpretation of the function of language in this group of neurotic and hysterical patients based on the foregoing discussion is as follows: Language is used primarily as a medium for self-expression and pointed communication, and less to provide a third dimension, content material, for mutual consideration by speaker and listener. Egocentricity, a restriction of the flow of ideas away from a given focus, less attentiveness to discrimination and qualification, emphasis upon actions and relations rather than on objects, and time orientation in the immediate present are suggested by the language patterns.

CONCLUSION

The focus of this paper is mainly on the study of language as an available objective tool for validation and exploration of psychological traits. The present study suggests that this is possible and that certain characteristics of language behavior point to parallel characteristics in psychological make-up. A descriptive evaluation is given of the language behavior of a subgroup of the psychoneuroses (hysteria) as distinct from that of the "normal" pattern. It appears from our findings that the language pattern of "neurotic" patients shows a significant relative increase in the use of verbs and pronouns and a significant relative decrease in the use of substantives, adjectives, prepositions, conjunctions, and articles. In the 10 most frequently used words, "neurotic" language patterns differ from "normal" patterns in the use of the pronouns "it" and "you" and in substitution of "is" for "was." The incidence of the pronoun "I" is significantly higher in "neurotic" language. Significantly fewer different words are used per thousand.

PROGNOSIS OF NEUROLOGIC ILLNESS FOLLOWING VACCINATION AGAINST SMALLPOX

HENRY G. MILLER, M.D., F.R.C.P.
Newcastle upon Tyne, England

THE IMMEDIATE mortality of encephalomyelitis following Jennerian vaccination is usually stated to be in the region of 30 to 50%. The mortality has, however, tended to be lower in recent series. Greenberg and Appelbaum,[1] for example, report 46 neurologic illnesses following approximately 5,000,000 vaccinations in New York City in 1947, with 8 deaths, 4 of which were due to coincidental disease, such as tuberculous meningitis or coronary thrombosis. The remaining four deaths were probably encephalitic, though the classic histopathological changes were lacking.

As regards the remote prognosis, it is commonly stated that recovery from postvaccinal encephalomyelitis is usually remarkably complete and that residual symptoms are exceptional,[2] though, in fact, accounts of the subsequent fate of patients recovering from the acute illness are scanty. Most of the standard textbooks indicate a low incidence of sequelae—"complete recovery is the rule" [3]; "recovery is usually complete" [4]; "in patients who recover residual disturbances are unusual" [5]—while Russell [6] goes so far as to cast doubt on the original diagnosis in cases in which residual mental changes or epilepsy has been reported. This view is supported by Kudelka,[7] who describes complete recovery in 27 cases of postvaccinal encephalitis in childhood. Ford,[8] however, speaks of an "astonishing tendency to recovery" but mentions mild spastic pareses and mental backwardness following the illness in patients personally observed, and he cites Krause,[9] who described hemiparesis,

From the Royal Victoria Infirmary, Newcastle upon Tyne, and the Ministry of Pensions, Northern Region.

1. Greenberg, M., and Appelbaum, E.: Postvaccinal Encephalitis: Report of 45 Cases in New York City, Am. J. M. Sc. **216**:565, 1948.

2. Brain, W. R.: Diseases of the Nervous System, Ed. 4, London, Oxford University Press, 1951, p. 502.

3. Wilson, S. A. K.: Neurology, London, Edward Arnold & Co., 1940, Vol. 1, p. 65.

4. Grinker, R. R., and Bucy, P. C.: Neurology, Ed. 4, Springfield, Ill., Charles C Thomas, Publisher, 1949, p. 671.

5. Friedewald, F. W., in Principles of Internal Medicine, edited by T. R. Harrison, Philadelphia, The Blakiston Company, 1950, p. 1055.

6. Russell, F. F., in Oxford Loose-Leaf Medicine, edited by H. A. Christian, New York, Oxford University Press, 1942.

7. Kudelka, O.: Nachuntersuchung von 27 Fällen postvakzinaler Encephalitis, München, med. Wchnschr. **79**:379, 1932.

8. Ford, F. R.: Diseases of the Nervous System in Infancy, Childhood and Adolescence, Ed. 2, Springfield, Ill., Charles C Thomas, Publisher, 1944, p. 603.

9. Krause, F.: Klinische Mitteilung über schwere Defektzustände nach Encephalomyelitis postvaccinalis, Deutsche Ztschr. Nervenh. **114**:214, 1930.

choreoathetoid movements, and intellectual defect among sequelae seen in four recovered children. Armstrong [10] reports minor epilepsy and mental deterioration, and Greenberg and Appelbaum [1] describe the occurrence of hemiparesis and "optic neuritis" under similar circumstances.

The present report is based on the medical records, furnished by the Ministry of Pensions, of 31 service men who had neurologic illnesses following vaccination during the period between 1939 and 1946, inclusive. Three cases of poliomyelitis which developed on the third and fifth days after primary vaccination and on the seventh day after revaccination respectively are excluded, as is one case of fatal encephalitis following primary vaccination and concurrent herpes zoster, which was considered on histopathological evidence to be one of zoster encephalitis. The remaining 27 cases comprise 3 of transverse myelitis, 16 of a purely encephalitic syndrome, 5 of encephalomyelitis in which encephalitic symptoms were associated with signs of involvement of the spinal cord or nerve roots, and 3 in which signs of a focal cerebral lesion arose without unequivocal symptoms of encephalitis. The 19 surviving patients in this series have all been subject to periodic neurologic examinations up to the time of this report.

FATAL CASES

In eight of the 27 cases of postvaccinal encephalomyelitis death occurred within 12 hours to 8 days after the onset of symptoms. The intervals between vaccination and onset of symptoms in these cases were 2, 5, 6, 8, 10, 11, 15, and 16 days; the durations of the illness were 12 hours, 12 hours, 36 hours, 36 hours, 5 days, 18 hours, 36 hours, and 8 days respectively. In all but one case the patients had been vaccinated for the first time; in two cases typhoid-paratyphoid had been given concurrently.

For the purpose of the present paper these cases do not justify individual consideration. In all the illness was encephalitic in its incidence. Four patients were found comatose or dead in bed after little or nothing in the way of premonitory symptoms. In the remaining patients fatal coma was heralded by malaise lasting a few hours, or at the most one or two days. Headache, meningism, incontinence, and flaccid paralyses with extensor plantar responses were usual features; three patients had convulsions. Other symptoms recorded included ptosis, ophthalmoplegia, sluggish pupils, trismus, abdominal pain and vomiting, and urticaria. All the patients died in coma, and none of those so treated showed convincing evidence of improvement following transfusion or injection of serum or blood from patients recently vaccinated.

CASES OF RECOVERY

In 19 cases the illness was followed by recovery; in all but 2 cases neurologic symptoms followed primary vaccination. In one case typhoid-paratyphoid inoculation, and in one case, typhoid-paratyphoid, tetanus toxoid, and antityphus inoculations, were carried out concurrently with vaccination. The intervals, expressed in days, between vaccination and the onset of neurologic symptoms were 2 (two cases), 3, 5, 7, 8 (two cases), 10 (five cases), 11, 12 (two cases), 14 (two cases), and 21, respectively, with an average incubation period of about 9 days, as in the fatal group. In 8 of the 19 cases of recovery the symptoms were purely encephalitic;

10. Armstrong, C.: Post-Vaccination Encephalitis, Ann. Int. Med. **5**:333, 1931.

5 were cases of encephalitis with coincident evidence of involvement of the cord; in 3 the illness was purely myelitic, and in 3 there were symptoms of a focal cerebral lesion without clinical encephalitis. In a case of probable latent encephalitis lethargica, a postvaccinal cerebral illness produced the appearance of a Parkinsonian syndrome.

Myelitis

Case 1.—*High transverse myelitis 10 days after primary vaccination; good recovery, but some residual disability 11 years later.*

A man aged 30 had an initial typhoid-paratyphoid inoculation and primary vaccination against smallpox in December, 1941. Ten days later a fever developed, without headache or meningism, and during the course of 24 hours he had symmetrical weakness of all four limbs, with retention of urine, extensor plantar responses, and patchy sensory loss up to the level of the clavicles. Improvement began within six weeks, sensory loss disappearing first; and he was discharged from the hospital four months later, able to walk short distances. In 1943 he had an unexplained epileptic convulsion in the absence of any relevant past history and without any recurrence up to the time of the present report. On reexamination, in 1951, he stated that he was working as a laborer and losing very little time from his work, but he still had some discomfort on walking long distances and still showed bilateral extensor plantar responses, with some increase in tone in both legs, more marked on the right.

Case 2.—*Low transverse myelitis 10 days after primary vaccination, with relatively mild symptoms at the onset, but with appreciable persisting disability 8 years later.*

A man aged 20 was vaccinated in January, 1944. Ten days later there developed headache and fever, and over the course of 24 hours weakness of the legs appeared, with numbness up to the groins and slight dysuria. He rested for two days and then returned to duty, but from this time onward he noticed weakness and stiffness of the legs on marching. Neurologic examination 12 months later showed spastic paraplegia with extensor plantar reflexes and absence of abdominal responses, patchy impairment of superficial sensation, and peripheral impairment of proprioceptive sensation. Two years after the onset reexamination showed persisting spasticity, slight unsteadiness of gait, and less extensive, but still distinct, sensory loss. At this time the plantar response on the left was still extensor in type, and that on the right was still equivocal, while ankle clonus persisted on the left side. The abdominal responses had returned. At the time of this report, eight years after the onset, he is still appreciably disabled after walking more than a mile.

Case 3.—*Transverse myelitis seven days after primary vaccination; trivial disability two years later.*

A sailor aged 21 was vaccinated for the first time in December, 1939. Seven days later an acute transverse myelitis developed, associated with headache, but without meningism. There were appropriate reflex changes and sensory loss, indicating an incomplete transverse lesion at the level of the fourth thoracic segment. The spinal fluid was normal. Improvement began within three weeks, and within four months there was fair recovery. At this time the patient was invalided with spastic paraplegia, sensation being normal. He was walking well, and his only complaints were urgency of micturition and inadequate emptying of the bladder.

Two years later the abnormal signs referable to the nervous system had completely disappeared, and his sole disability was occasional bed wetting, which had never occurred before the illness.

Encephalomyelitis

In five cases encephalitic symptoms were accompanied by evidence of involvement of the cord or nerve roots, and in three of these there were psychiatric sequelae.

Case 4.—*Moderately severe encephalomyelitis eight days after primary vaccination. Minor physical disability and residual signs persist eight years later.*

A man aged 26 was vaccinated in June, 1944. Eight days later there developed limb pains, headache, nausea, and vomiting. He was mentally confused for three days and incontinent for one week. On recovery from his mental confusion, he had tinnitus in the right ear, diplopia,

pain with hyperalgesia over the right side of the face and the outer side of the right thigh, and absence of the ankle jerk on the right side. During recovery unsteadiness of gait, backache, headaches, occasional vomiting, and excessive sweating of the right hand were present, and for several months he complained of poor memory and slowness in thinking.

Eighteen months after the initial illness he was still having occasional headaches and syncopal attacks, from which he had never suffered before. He still had occasional spasms of pain in the right side of the face and tingling on the outer side of the right thigh, while the skin over both these areas was unduly painful on gentle stimulation. There was blunting of sensation over the right thigh, and the ankle jerk was sluggish on this side.

For two years after the acute illness the patient's symptoms were complicated by an anxiety state, which arose in the absence of any predisposition to neurosis and which slowly cleared.

At the time of writing, eight years later, his chief symptoms are those of sensory discomfort in the face and right leg. The association of the leg symptom with backache and depression of the ankle jerk raised the suspicion that the symptoms in the right lower limb might be related to trauma sustained during lumbar puncture, but the coincidence of similar symptoms in the face renders their relation to the initiating disease more likely. His present disability is slight.

CASE 5.—*Encephalomyelitis 14 days after primary vaccination, followed by personality change, clinically evident intellectual impairment, and attacks of loss of consciousness; good recovery within three years.*

Fourteen days after primary vaccination this very efficient 19-year-old paratroop noncommissioned officer had high fever and severe headache. He was drowsy, with nuchal stiffness, flaccid quadriplegia with generalized depression of deep reflexes, absence of abdominal responses and an extensor plantar reflex on the left and an equivocal one on the right. The spinal fluid was under high pressure and contained 70 mg. of protein per 100 cc. and 121 lymphocytes per cubic millimeter. For four days he was comatose, with retention of urine. Consciousness became clear within six days; bladder control returned in eight days, and he was able to walk two weeks from the onset.

Two months later he still had frequent headaches, paresthesia down the trunk and limbs on bending the neck forward, and difficulty in thinking, remembering, and concentrating. He was facile in manner. There was patchy hyperesthesia, but no other abnormality referable to the nervous system except for absence of the lower abdominal reflexes and a patch of numbness on the left buttock. He was easily confused and unable to recall the date of his call-up or his service number.

Four months from the onset there were no objective residua. Headaches persisted, but paresthesia on forward flexion of the neck had disappeared. On four occasions severe headaches had been succeeded by loss of consciousness without frank epileptic features. Four months later there had been no further attacks of loss of consciousness, but he was still emotionally unstable, irritable, and aggressive, continually and inconsistently rambling about his combat experiences.

Twelve months later improvement continued, and he was working regularly as a carpenter, still intermittently depressed and unstable. Three years from the onset he had made a perfect recovery except for intermittent headaches. He appeared to have recovered his previous occupational efficiency and had no personality difficulties.

CASE 6.—*Mild encephalomyelitic syndrome 14 days after primary vaccination, and at the time of multiple inoculations; residual paraplegia, causing slight disability 5 years later.*

On Feb. 2, 1945, a soldier aged 17 was vaccinated for the first time and was simultaneously inoculated with typhoid-paratyphoid vaccine, tetanus toxoid, and antityphus vaccine. On Feb. 9 and Feb. 14 he had further antityphus inoculations, and on the latter date he became drowsy and felt weak in the limbs. The next day drowsiness had disappeared, but weakness and spontaneous nocturnal twitching of the legs, with numbness and tingling in the hands, persisted, and three weeks later he reported these symptoms to his medical officer. Examination revealed spastic paraplegia, more pronounced on the left, without sensory change, sphincter involvement, or evidence of cerebral involvement.

Twelve months later these signs persisted, and he still complained of a "dead feeling" in his left hand, unassociated with objective sensory or other changes. Three years later symptoms related to the left hand had disappeared, and five years after the onset of symptoms disability from the residual paraplegia was slight.

CASE 7.—*Myelitic syndrome 10 days after primary vaccination; apparent recurrence of the illness, with mild encephalitic symptoms and apparent increase of physical signs, 6 months later. Twelve years later a partial Brown-Sequard syndrome persists, complicated by psychoneurosis and hypertension.*

A man aged 28, of low intelligence, was vaccinated in November, 1939. Ten days later he complained of headache, limb pains, and numbness of the legs. The spinal fluid was found to be normal, and, despite signs of spasticity on the left side with an extensor response and patchy sensory loss below the waist, a diagnosis of hysteria was made and he was returned from a civilian hospital to his unit four days later.

Six months later he was readmitted to the hospital with headache, drowsiness, and apparently increased signs of a left-sided lesion of the spinal cord at the 10th thoracic segment. He was afebrile, and recovery from his general symptoms was rapid, though the focal signs persisted.

Reexamination three and five years after the illness showed multiple complaints of a hysterical nature, with marked hypochondriasis. Spasticity of the left leg, with superficial sensory loss in the right, persisted, reflex changes were as before, the left plantar response remaining extensor.

Twelve years after the illness the signs were similar except that the left plantar response was now flexor. Hypochondriasis persisted; he was then hypertensive, and he complained of increasing numbness and weakness in the right and left legs respectively, though such objective change as could be detected was in the direction of improvement.

CASE 8.—*Moderately severe encephalomyelitis 10 days after primary vaccination, with residual symptoms of paraplegia and anxiety.*

A man aged 31 was vaccinated in June, 1943. Ten days later there developed fever, headache, nuchal stiffness, urinary retention, and mental confusion, proceeding to stupor. Consciousness returned within 36 hours, but he was left with generalized pains and was paraplegic and incontinent of urine and feces for three weeks. The spinal fluid contained 100 lymphocytes per cubic millimeter, and the protein content was normal. Improvement was rapid, and within six months of the onset he could walk nearly a mile.

Two years later he still had stiffness and pain in the legs after walking. Five years from onset of the illness this had disappeared; power and reflexes were normal, and his only relevant symptoms were frequency of micturition and relative impotence.

The patient's early history showed evidence of inadequacy and neurotic predisposition, he exhibited persisting psychiatric sequelae of mixed anxiety and hysterical type.

ENCEPHALITIS

Nine patients recovered from encephalitic illnesses; in only one did the condition appear comparable in severity with that in the cases of fatal encephalitis described above. In six of these patients there were psychiatric sequelae.

CASE 9.—*Severe encephalitis 10 days after primary vaccination; sequelae of psychoneurotic pattern, with slow improvement over the course of several years.*

Ten days after vaccination a soldier aged 21, of low intelligence, complained of intense headache and became mentally confused and subsequently comatose, with nuchal stiffness. He was admitted to the hospital with the diagnosis of cerebrospinal meningitis, but the spinal fluid proved to be normal. He was unconscious for over a week but recovered without focal signs. He returned to his unit six weeks later but complained so bitterly of headaches, backache, and sleeplessness that he was invalided a few months later as psychoneurotic. There was never any evidence of organic intellectual impairment, but the severity of the initial illness, the consistency of his symptoms in the absence of previous overt psychiatric disability, and the steady improvement which subsequently occurred led later observers to consider his symptoms as organically determined by the encephalitis. Seven years after the illness his disability was trivial, and his symptoms were those of a mild chronic anxiety state.

CASE 10.—*Encephalitic illness 11 days after primary vaccination; past history of probable hysterical symptoms; possible recurrence of encephalomyelitis three months later. Minor organic signs, emotional symptoms, and personality change, with severe disability, persisted three years later.*

For several years a soldier, aged 24 at the time of this report, had occasionally reported sick, complaining of loss of use of the legs and double vision. Objective signs had always been lacking, and the patient had been regarded as a hysterical personality of poor morale, a view supported by formal psychiatric assessment at a later date. Eleven days after primary vaccination in February, 1944, high fever, headache, and mental confusion developed, and he complained of numbness of the hands and feet. Examination revealed meningism, generalized hyperesthesia, and right hemiparesis, with an equivocal plantar response; the spinal fluid was normal. Consciousness became clear on the third day, and at the same time dysarthria was noted. He was discharged from the hospital in three weeks with slight weakness of the lower right side of the face, some slurring of speech, and a rather apathetic manner. Episodic headaches persisted. Three months later he had a more intense headache and became drowsy. On readmission to the hospital, he was afebrile and dysarthric, with clouded consciousness, poor palatal movements, and slight spasticity of the right side. The differential diagnosis lay between a recurrence of encephalomyelitis and hysteria. Headache and clouding of consciousness cleared within three days. The patient's behavior, however, was abnormal. He was retarded, was full of self-pity, and persistently refused food. Little improvement occurred over the course of four months, and the patient was invalided.

On reexamination three years later, the right hemiparesis was no longer detectable, but dysarthria remained and the patient was severely disabled by episodic headaches, chronic apprehension, and poor memory and concentration.

CASE 11.—*Encephalitic episode 14 days after primary vaccination, associated with a major convulsion. Physical signs rapidly cleared, but headaches and major epilepsy ensued.*

Fourteen days after primary vaccination a soldier aged 18 was noticed to have put on the wrong uniform and to be dazed and slow in his movements. On being questioned, he complained of headache, of several hours' duration, and fell to the ground in a major epileptic convulsion. On recovery he was mentally confused, with meningism, an extensor plantar response on the right, and normal spinal fluid. The condition became worse over a period of 24 hours; spontaneous nystagmus developed, and both plantar responses became extensor. Within seven days, however, the symptoms and abnormal signs had completely disappeared. The patient returned to duty and made no complaint until two months later, when, after several nights' loss of sleep on maneuvers, he had a second major fit. During the subsequent three years he had about four fits annually and a severe generalized headache about once a month. Seven years after the illness, however, headaches had disappeared, and the fits were almost completely controlled by barbiturates. Careful inquiry has failed to reveal any relevant past or family history of epileptic manifestations.

CASE 12.—*Brief attack of encephalitis 10 days after primary vaccination; possible relapse 15 days later, again with recovery. In a basically hysterical personality, gross hysterical sequelae have been accompanied by occupational and social deterioration.*

An ex-pugilist and film-stunt artist aged 31, in 1941 was admitted to the hospital, 10 days after primary vaccination, with high fever, headache, "syncopal attacks," and mental confusion. There were no focal signs. Four days later he had recovered. While on leave 15 days later, he had a convulsion and exhibited gross generalized hypotonia and ataxia; his condition was diagnosed by an experienced neurologist as encephalomyelitis. He was readmitted to the hospital and again showed improvement within a week. Two grossly hysterical fits 10 days later led to his transfer to a psychiatric hospital, and he was invalided with the diagnosis of hysteria. There was, despite his personality, no evidence of any preceding manifest psychiatric disability, and the patient's subsequent deterioration led first to a diagnosis of encephalitis lethargica and subsequently, in view of failure of any of the familiar postencephalitic features to develop, to a diagnosis of organically determined degenerative hysteria following postvaccinal encephalomyelitis. Most of his symptoms have been vague and subjective—intermittent weakness of the arms and legs (without abnormal physical signs), headaches, loss of interest and concentration, irregular tremor of the head and right arm, and slurred speech. Psychometric tests have not been carried out, but the patient's severe disability and a marked decline in his social and occupational status support a clinical diagnosis of personality change, if not of organic intellectual deterioration.

CASE 13.—*Mild attack of encephalitis seven days after primary vaccination; rapid recovery, with obstinate sequelae of psychoneurotic pattern persisting nine years later.*

Seven days after primary vaccination a soldier aged 26, in whose personal and family background there was no evidence of predisposition to neurosis, had onset of headache, backache, fever, vomiting, and photophobia. He was drowsy for 36 hours, with nuchal stiffness, but the spinal fluid was normal. Recovery was rapid but headaches and severe anxiety symptoms followed immediately. He overheard a remark which led him to believe he had had meningitis and became very "head-conscious" and hypochondriacal. After eight months in the hospital, he was invalided on psychiatric grounds. Twelve months after being invalided he was still very disabled by headaches and emotional symptoms. Four years after the illness he was working as bus driver, but he was still frequently incapacitated by headaches and dizziness and was introspective and sleepless, with frequent nightmares. Nine years after the illness these symptoms were less severe but still caused occasional absence from work.

CASE 14.—*Mild encephalitis following primary vaccination; subsequent minor psychoneurosis.*

A man aged 37, who was suffering from apparently psychoneurotic sequelae of a very minor head injury six months previously, had fever, photophobia, headache, and diplopia in all directions of gaze 10 days after vaccination. The spinal fluid was normal, and he was well within five days except that his double vision persisted for six weeks. Consciousness was never clouded. After the illness anxiety symptoms developed, and he was invalided, partly in view of severe domestic stress and partly because of the appreciable predisposition to neurosis evident in his history. There was never any evidence of personality change or deterioration, and, although hypochondriacal attitudes and symptoms persisted, his residual disability two years later was trivial.

CASE 15.—*Mild encephalitic illness five days after primary vaccination; good recovery except for symptoms probably the result of lumbar puncture.*

Five days after vaccination a man aged 19 had onset of fever, headache, trismus, and nuchal stiffness. Consciousness was not clouded. The spinal fluid was normal, but after lumbar puncture pain in the back and down the right leg developed, with some difficulty in micturition. The latter symptom disappeared within a month, but headaches and pain in the back and down the leg were still occasionally troublesome two years later.

CASE 16.—*Mild encephalomyelitis 12 days after revaccination against smallpox and typhoid-paratyphoid inoculation; Parkinsonian symptoms noticeable a month later; history of probable lethargic encephalitis 12 years previously. Attack of postvaccinal encephalomyelitis apparently produced exacerbation of latent encephalitis lethargica.*

A man aged 26 had major and minor epilepsy in childhood; the seizures cleared up completely after a very severe illness, at the age of 14 (1928), during which he was drowsy and mentally confused for many weeks. He made a good recovery, but since this time, though he had been employed in heavy unskilled work, he was generally considered unstable and inadequate. He complained of frequent attacks of poorly localized pain, sometimes "collapsed" at work, and had frequent periods of invalidism, with "nervous debility" and depression. However, he joined the army in Grade I and on July 8, 1940, was revaccinated (there was a history of successful vaccination in infancy) and inoculated with 1 cc. of typhoid-paratyphoid vaccine. Twelve days later fever, drowsiness, and intense headache developed. He was semistuporous and amnesic on admission to hospital, showing flaccid left hemiparesis, with absence of deep reflexes but a flexor plantar response. The spinal fluid was normal. He remained very ill and febrile for 48 hours, subsequently improving. During convalescence he complained of headaches, difficulty in thinking and concentration, and vacant, "staring" attacks. On return to his unit a month after the illness, Parkinsonian symptoms were evident—characteristic facies, infrequent blinking, bilateral pill-rolling movements, and emotionalism. He was invalided, and since that time his post-encephalitic Parkinsonism has slowly deteriorated.

FOCAL CEREBRAL LESIONS WITHOUT ENCEPHALITIC FEATURES

In three patients focal cerebral lesions developed after vaccination at intervals of 2, 3 and 21 days respectively. Only one of these patients (Case 18) exhibited any symptoms suggestive of more diffuse cerebral disease.

CASE 17.—*Acute focal lesion of the brain stem developing two days after primary vaccination for smallpox and inoculation with typhoid-paratyphoid vaccine and tetanus toxoid. Improvement rapid; no further episodes, but persisting signs five years later.*

A youth aged 17 was vaccinated for smallpox and given 1 cc. of typhoid-paratyphoid vaccine and 0.5 cc. of tetanus toxoid intramuscularly on the same day. Two days later he reported sick, with vertigo and blurred and double vision, of sudden onset. There was only slight headache, and no fever, meningism, or disturbance of consciousness; the spinal fluid was normal. Examination showed strabismus, probably due to a lesion of the left abducens nerve. Hypalgesia was present over the left side of the face, maximal centrally, with absence of the left corneal reflex, and also over the right side of the body between and including the sixth thoracic and the third lumbar dermatome. Nystagmus was present questionably. The right hand was weak, and abdominal responses could not be elicited on the right; but there were no abnormal signs in the legs. Deep sensibility was everywhere normal. The diagnosis of an acute hemilesion of the brain stem was made, and several diagnostic possibilities were discussed, namely, syringomyelia, hematomyelia, focal postvaccinal encephalomyelitis, and multiple sclerosis. Improvement was rapid, particularly in the diplopia, which cleared within a few days. Five years later, at the time of writing, occasional parethesias and sensory blunting persist in both the affected areas, while the right hand remains slightly clumsy for fine movements. There have been no further neurologic developments.

CASE 18.—*Acute cerebral illness with massive cerebral lesion three days after revaccination, with motor aphasia and hemiplegia. Nine years later hemiplegia, choreoathetoid movements, epilepsy, and personality changes still totally incapacitating.*

In April, 1942, a soldier aged 22 was admitted to the hospital with bacillary dysentery. Three days after revaccination, carried out in view of a local epidemic, he became confused and drowsy, complained of headache, and had onset of acute right hemiplegia with motor aphasia. The spinal fluid was normal. The aphasia improved within 10 days, though he was dysphasic for 4 months; but the hemiplegia persisted, and 16 months after the illness focal epilepsy developed. Attacks always began in the right hand but often progressed to a generalized convulsion. There have been no organic mental changes, but now, nine years later, the patient still has severe hemiparesis, epilepsy, choreoathetoid movements of the right hand, and hypochondriasis.

CASE 19.—*Sudden hemiplegia three weeks after primary vaccination; three years later persisting hemiparesis, complicated by marked emotional and personality changes. Nine years after the illness slight hemiparesis was the only disability.*

Three weeks after primary vaccination a soldier aged 18 became giddy and, while throwing a grenade, fell to the ground, with weakness of the left side of the body. He recovered in 30 minutes but had a recurrence of symptoms an hour later, which were much severer. There was no impairment of consciousness, headache, or abnormality of the spinal fluid. Slow improvement, over 18 months, was complicated by pronounced personality changes. Previously stable and efficient, he became irritable, timid, and hypochondriacal, with poor morale and multiple trivial complaints. These symptoms persisted three years after the illness, but they were improving; nine years after the onset left hemiparesis, troublesome in cold weather, was the only disability.

COMMENT

The value of this series of cases as a basis for the statistical study of prognosis is vitiated by the source from which it is drawn—the medical records of the Ministry of Pensions. Apparently unselected, these cases are in fact a selected group, in that every surviving patient at some stage received a pension for disability resulting from neurologic illness following vaccination. While the series probably includes every fatal case of postvaccinal encephalomyelitis occurring in the services between 1939 and 1946, it is possible that cases of similar illness in which recovery occurred without sequelae, or at any rate without resulting in a claim for residual disability, have been omitted.

That the present series may, however, be more representative than this qualification would imply is suggested by figures provided by one of the fighting services

at risk during this period (personal communication). Among 1,750,000 personnel members vaccinated between 1941 and 1950, 10 had postvaccinal encephalomyelitis (an incidence of 1 in 175,000 vaccinations), with 3 deaths. The mortality is, in fact, identical with that reported in the present series, and if, as seems likely, the two series of patients are comparable, the present paper may be regarded as giving some indication not only of the nature and duration of sequelae but also of their frequency.

Prognosis.—If one bears in mind the possible omission of milder cases, the mortality rate in the present series is in keeping with that previously reported. Death occurred in 8 of 27 cases (30%). If the three cases of transverse myelitis and the three cases of focal cerebral accidents are excluded, the mortality for true encephalomyelitis rises to 38%.

Neither length of incubation period nor any group of focal signs can be correlated with prognosis. The fatalities, however, were entirely among patients with encephalitic symptoms, and it would appear that the degree of disturbance of consciousness is related to prognosis. Of 10 patients who became comatose, only 2 survived (Cases 5 and 9). Of four patients with convulsion in the acute illness, only one survived (Case 11).

Relapse and recurrence are familiar features of acute disseminated encephalomyelitis, and the former has been reported in cases of postvaccinal encephalomyelitis by Greenberg and Appelbaum.[1] In the present series, neither the case of relapse after 15 days (Case 12) nor the cases of recurrence after three and six months respectively (Cases 7 and 10) are entirely convincing. In Cases 10 and 12 there was positive evidence of hysteria before and after the illness, while in Case 7 a relapse which cannot be accepted as unequivocally organic occurred in a psychoneurotic subject of low intelligence.

Focal Cerebral Accidents.—The nature of the focal cerebral lesions which followed vaccination in Cases 17, 18, and 19 is obscure. In only the second of these cases does the history suggest that the focal lesion may have been part of a more diffuse cerebral disease. The abrupt onset and subsequent improvement in these cases suggest a vascular origin. The occurrence of similar syndromes in the course of convalescence from specific fevers is well recognized; sometimes arising during the course of clearly encephalomyelitic illnesses, they are at other times isolated incidents. Clinical evidence suggests the possibility of a common pathogenesis for such syndromes whether they form part of a general cerebral illness or occur in isolation. Infiltrative vasculitis has been described in pathological studies of acute disseminated encephalomyelitis by many observers.[11] Whether or not these vascular changes are an index of the central role of allergic vasculitis in the production of

11. Barlow, T.: On a Case of Early Disseminated Myelitis Occurring in the Exanthem Stage of Measles and Fatal on the Eleventh Day of That Disease: Report on the Microscopical Examination of the Spinal Cord, Tr. Med. Chir. Soc. London **70**:77, 1887. Bergenfeldt, E.: Myelitis als Masernkomplication, Acta med. scandinav. **61**:281, 1924. Perdrau, J. R.: Histology of Post-Vaccinal Encephalitis, J. Path. & Bact. **31**:17, 1928. Wohlwill, F.: Über Encephalomyelitis bei Masern, Ztschr. ges. Neurol. u. Psychiat. **112**:20, 1928. Alpers, B. J.: So-Called "Brain Purpura or "Hemorrhagic Encephalitis": Clinicopathologic Study, Arch. Neurol. & Psychiat. **20**:497, 1928. Hassin, G. B.: Disseminated Encephalomyelitis (Meningoencephalomyeloradiculitis) Versus Multiple Sclerosis, ibid. **40**:111, 1938. Scheinker, I. M.: Neuropathology in Its Clinicopathologic Aspects, Springfield, Ill., Charles C Thomas, Publisher, 1947.

acute disseminated encephalomyelitis, as I have suggested,[12] it is clear that they are a common pathological finding, and it is possible that some such inflammatory arterial or venous lesion, possibly complicated by thrombosis, may be responsible for some of the hemiplegic and similar syndromes under consideration. The solution to this problem depends on more careful histopathological examination of arteries and veins in the occasional fatal cases of this kind, and, indeed, in other cases in which fatal cerebral accidents occur in the absence of degenerative arterial disease.

Organic Sequelae.—Although none of the surviving patients gave evidence of subsequent multiple sclerosis or of any progressive nervous disease, an unexpected finding is the high incidence of subsequent morbidity of an unequivocally organic nature, including hemiplegic and root syndromes, dysarthria, involuntary movements, and epilepsy.

In all three cases of transverse myelitis there was fair recovery, with residual disability, and in two cases residual signs. This outcome is in keeping with general experience. Of the five cases of encephalitic syndromes with associated signs of involvement of the spinal cord or nerve roots, residual organic signs and disability were present some years later in three, while in all three cases of focal cerebral illness appreciable disability remained. In the nine cases of purely encephalitic illnesses, however, residual physical signs were exceptional.

Of the cases in which epilepsy occurred after recovery, focal epilepsy followed hemiplegia in one (Case 18), and major fits accompanied and followed an attack of encephalomyelitis unassociated with evidence of gross focal brain damage in another (Case 11). Electroencephalographic studies in this case might have helped to reveal constitutional and acquired factors in the epilepsy, but they were not carried out. There seems nothing inherently improbable in the occasional activation of latent dysrhythmia by an encephalitic illness. In other cases attacks of loss of consciousness of less certain epileptic type followed the illness, and some such attacks may well have been of a similar nature. They are not uncommon after other forms of encephalomyelitis, and from personal observation of their occurrence after spontaneous or postinfective illnesses the prognosis for cessation of such attacks appears to be good, as in the cases described in this paper.

Psychiatric Sequelae.—The incidence of psychiatric sequelae is of interest, and these syndromes present the same difficulty of assessment as do the similar sequelae of head injury, meningitis, or, indeed, any other organic cerebral illness. Of the 12 cases of recovery from encephalitic syndromes, subsequent psychiatric symptoms developed in 9. The absence of such symptoms in the three cases of myelitis may, of course, be coincidental, in view of the small numbers involved, but it is more probable that, whether or not the psychiatric symptoms are organically determined, they are more likely to follow an illness affecting the higher levels of the nervous system.

Gross intellectual impairment is a familiar, if uncommon, sequel of post-exanthematous encephalomyelitis in childhood. The only unequivocal instance encountered in the present series was Case 5, in which transient intellectual impairment and personality change followed severe encephalomyelitis in a patient without

12. Miller, H. G.: Clinical Consideration of Cerebrovascular Disorders Occurring During the Course of General Diseases of an Inflammatory or Allergic Nature, Proc. Roy. Soc. Med. **44**:852, 1951.

positive evidence of predisposition to psychiatric illness. Another possible example of intellectual impairment, and a certain instance of personality deterioration, was Case 12, the only case in the series in which an apparently permanent decline in social and occupational status was caused by residual psychiatric symptoms. The cerebral illness in this case was not particularly severe, but the patient's previous personality showed evidence of abnormality in the form of gross hysterical tendencies, which similarly colored his subsequent symptoms.

In most cases there was nothing specifically organic in the nature of the psychiatric symptoms. In general, the disability appeared to represent the product of two factors—the severity of the cerebral illness, and the predisposition to psychoneurosis evident in the patient's earlier history. In this, as in other directions, the parallel with post-traumatic cerebral syndromes is close. In five of the nine cases with psychiatric sequelae there was clear evidence of material predisposition to neurosis—in two cases associated with subnormal intelligence and in one with severe complicating domestic stress. Of the four cases in which psychiatric sequelae developed in the absence of predisposition, the initial illness was severe in three (Cases 4, 5, and 9). Case 13 is unusual in that psychiatric symptoms persisted nine years after a relatively mild encephalomyelitis in the absence of evident predisposition to neurosis; the history of this case indicates that medical suggestion and the absence of positive reassurance at an early stage may have played a part in the perpetuation of symptoms.

The psychiatric picture in these cases was less clear-cut than is usual in the similarly problematic postconcussional or postcontusional syndrome, but the steady improvement recorded in all the cases, with the exception of Cases 10 and 12, in which there was gross hysteria, suggests an organic component, or at any rate that the organic cerebral illness was in some way the major factor in subsequent disability. From a survey of cases of spontaneous acute encephalomyelitis occurring in a civilian hospital, which has been carried out concurrently, there seems no doubt that the psychiatric sequelae in the patients in the present series are more frequent and severer than those observed in civilian patients with similar illnesses of apparently comparable severity.

Such a finding is, of course, almost invariable in disease of any kind among pensioners, as it is among patients whose disability is related to industrial risk or injury. In the former, for example, even peptic ulcer is an illness often associated with psychiatric complications or invalidism, a situation rarely encountered under other circumstances. This difference may be due in part to the necessity in such cases of the physician's assessing the patient's total disability, whereas in routine hospital practice emotional symptoms are not infrequently ignored as irrelevant to the major complaint. It is unlikely, however, that this factor alone accounts for the difference in incidence of psychoneurotic features, and there can be little doubt that in the cases at present under consideration knowledge of the cause of the disease, the additional emotional stresses of service life for the frequently reluctant soldier, and the probability of secondary gain from the illness were important factors in the psychoneurotic elaboration and perpetuation of symptoms that may originally have had an organic basis. It is likely that organic brain damage lowered the patient's threshold to environmental anxieties, but that secondary emotional mechanisms played a major part in the prolongation of the disability.

SUMMARY

This paper reports 27 cases of neurological illness following Jennerian vaccination. In 16 of these cases the disease was purely encephalitic; 5 were cases of encephalitis with associated signs of involvement of the spinal cord or nerve roots, 3, of transverse myelitis, and 3, of focal cerebral lesions without unequivocal evidence of encephalitis. In eight cases death occurred within hours or days of the onset of the illness; all these cases were drawn from the encephalitic group. Although residual organic signs of the illness were frequent and included paraplegic, hemiplegic, and radicular syndromes; dysarthria, epilepsy, and involuntary movements, in few cases was any serious physical disability found on reexamination after several years, and there were no instances of progressive nervous illness, except one of coincidental postencephalitic Parkinsonism. Psychiatric sequelae were common and oftener disabling.

The nature of the focal cerebral illnesses is discussed, and it is suggested that such illnesses may arise from thrombosis in arteries or veins which are the seat of inflammatory change. The respective roles of physical and emotional factors in the causation of psychiatric sequelae are considered.

The Director-General of Medical Services, Ministry of Pensions, permitted access to the records in these cases.

ELECTROENCEPHALOGRAMS OF NONEPILEPTIC PSYCHOTIC PATIENTS AWAKE AND ASLEEP

GEORGE LYKETSOS, M.D.

LOUIS BELINSON, M.D.

AND

F. A. GIBBS, M.D.

With the Technical Assistance of Anton Engel

CHICAGO

BECAUSE electroencephalographic studies on epileptics recorded during sleep reveal more significant abnormalities than those recorded in the waking state,[1] it seemed possible that electroencephalographic recordings during sleep on psychotic patients might reveal abnormalities that were nonevident in these patients when awake. However, this hope was somewhat dimmed by the fact that the sleep studies on psychotic patients of Hans Berger [2] and Liberson [3] had failed to reveal significant abnormalities. The latter was able to show differences in the proportion of drowsiness patterns in various types of mental diseases. Diaz-Guerrero, Gottlieb, and Knott [4] compared the entire night sleep records of six manic-depressive patients with six normal subjects but found no electroencephalographic features which might be of diagnostic value.

It was not the intention in the present study to continue the analysis of cases of psychomotor epilepsy and seizure discharges from the anterior temporal lobe, for a relation has already been demonstrated between seizure activity in the anterior temporal lobe and psychosis.[5] The incidence of psychosis has been shown to be generally related to the number, voltage, and bilaterality of spike seizure discharges

From the Jacksonville State Hospital and the Department of Neurology and Neurosurgery, University of Illinois School of Medicine.

1. Gibbs, F. A., and Gibbs, E. L.: Atlas of Electroencephalography, Ed. 2, Methodology and Controls, Vol. 1, 1950, and Epilepsy, Vol. 2, 1952, Cambridge, Mass., Addison-Wesley Press.

2. Berger, H.: Über das Elektrenkephalogramm des Menschen, Arch. Psychiat. **87:** 527-570, 1929; **94:**16-60, 1931; **97:**6-26, 1932; **98:**231-254, 1932; **99:**55, 1933; **100:**301, 1933; **101:**452-469, 1933; **102:**538-557, 1934; **103:**444-454, 1935; **104:**678-689, 1936; **106:**165-187, 1937; **106:**577-584, 1937; **108:**407-431, 1938.

3. Liberson, W. T.: Problems of Sleep and Mental Disease, Digest Neurol. & Psychiat. **13:**93-108, 1945; Functional Electroencephalography in Mental Disorders, Dis. Nerv. System **5:**357-364, 1944.

4. Diaz-Guerrero, R.; Gottlieb, J. S., and Knott, J. R.: The Sleep of Patients with Manic-Depressive Psychosis, Depressive Type: An Electroencephalographic Study, Psychosom. Med. **8:**399-404, 1946.

5. Fuster, B.; Gibbs, E. L., and Gibbs, F. A.: Anterior Temporal Localization of Sleep-Induced Seizure Discharges of Psychomotor Type; cited by Gibbs, E. L.; Gibbs, F. A., and Fuster, B.: Pyschomotor Epilepsy, Arch. Neurol. & Psychiat. **60:**331, 1948.

in the anterior temporal areas,[6] and it is known that these spike seizure discharges are best seen during natural or induced sleep.[5] Cases of clearly defined anterior temporal lobe spikes were therefore excluded from the present consideration. Rage attacks and behavior disturbances are positively associated with 14- and 6-per-second positive spikes, which appear in light sleep and are considered suggestive of thalamic or hypothalamic epilepsy.[7] Since it was not the purpose of the present study to proceed with a further analysis of such cases, cases of clearly defined 14- and 6-per-second positive spikes were also excluded. The question we sought to answer was this: Is there a relation between psychoses and electroencephalographic abnormality when recognized types of epilepsy are excluded?

PRESENT INVESTIGATION

Material.—A series of 100 nonepileptic patients with psychosis were selected. None had clinical evidence of epilepsy, and none had clearly defined anterior temporal lobe spikes or 14- and 6-per-second positive spikes. All patients had a very severe form of so-called functional psychosis; patients with both recent and chronic disease were included. Patients with physical illnesses were excluded, as were those who had received convulsive shock or insulin shock therapy.

The diagnostic classification of the patients was as follows: schizophrenia, 49; nonschizophrenic illnesses, 51. The schizophrenic group were divided as follows: simple type, 11; hebephrenic, 5; catatonic, 15; paranoid, 17, and undetermined, 1. The nonschizophrenic group comprised 16 patients with paranoid conditions, i. e., paranoia or paraphrenia; 11 with manic-depressive psychosis (7 in the depressed and 4 in the manic phase); 7 with involutional psychosis (5 of the melancholic and 2 of the paranoid type); 12 with a psychosis of unclassified type, and 5 with a psychosis which was presumably organic or toxic in origin.

Method.—Monopolar recordings from the frontal, anterior temporal, midtemporal, parietal, and occipital areas of both hemispheres [1] were made on a Grass six- or eight-channel electroencephalograph. Interconnected ear lobes were used as the reference, but when there was any question about the activity of the reference, one ear lobe, the nose, the chin, or the chest was used as the alternate reference. On all patients recordings were made both in the waking and in the sleeping states. In a few patients sleep was spontaneous, but in most it was induced with secobarbital (Seconal) or paraldehyde.

The standards of normality and abnormality for waking and sleep recordings were those described in the "Atlas of Electroencephalography." [1]

Results.—In general, the waking activity of the psychotic group was like that of normal control subjects (Fig. 1). When the psychotic group was subdivided into the schizophrenic (49 patients) and the nonschizophrenic (51 patients) subgroup, the former was found to contain a slightly higher proportion of patients with fast activity (Fig. 2). Small sharp spikes were rather common in the subgroup with paranoid psychosis, but no more so than in a control group of comparable age.

For comparison of differences in the voltage of sleep patterns in the various clinical diagnostic groups, sleep recordings were classified according to the general amplitude of activity during all phases of sleep. Examples of high-, medium-, and low-voltage sleep patterns are shown in Figure 3. As will be seen in Figure 4, low-voltage sleep patterns were commoner in the psychotic patients than in the normal control series. There was no correlation between low-voltage sleep activity and low-voltage waking activity; many patients with low-voltage sleep patterns

6. Lyketsos, G., and Gibbs, A.: Psychosis and Psychomotor Epilepsy, to be published.

7. Gibbs, E. L., and Gibbs, F. A.: Electroencephalographic Evidence of Thalamic and Hypothalamic Epilepsy, Neurology **1**:136-144, 1951.

had high-voltage dominant alpha activity in the waking state. Age factors were not responsible for the lower-voltage sleep pattern of the psychotic patients.

The mittens pattern, a sleep pattern which was first described by Leemhuis and Stamps,[8] and which these authors reported as particularly common in patients with Parkinsonism, was found in the present group of psychotic patients (Fig. 5).

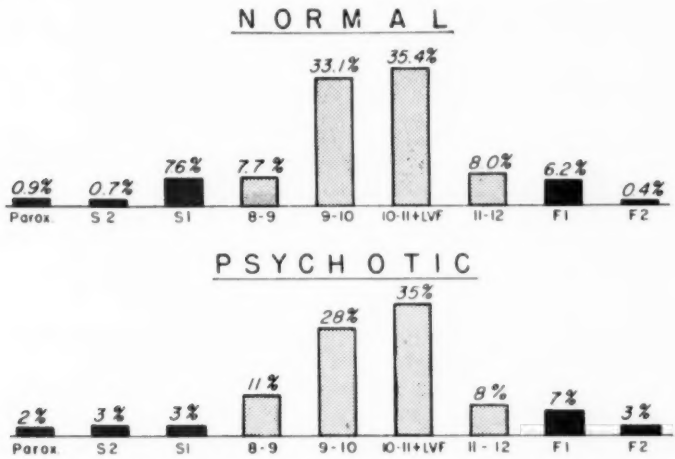

Fig. 1.—Waking activity of normal controls and psychotic patients.

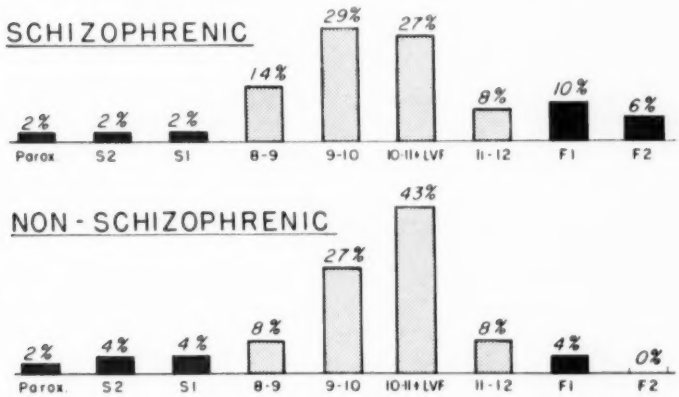

Fig. 2.—Incidence of fast activity in patients with schizophrenic and nonschizophrenic psychoses.

It usually occurred in association with 6- to 10-per-second spindles in the frontal areas, but in less highly developed form it often appeared synchronously (with frontal mitten pattern) in the parietal areas. A comparison of the incidence of

8. Leemhuis, A. J., and Stamps, F.: Mittens Patterns in Electroencephalograms of Patients with Parkinsonism, read before American Electroencephalographic Society Meetings, Atlantic City, N. J., June, 1949.

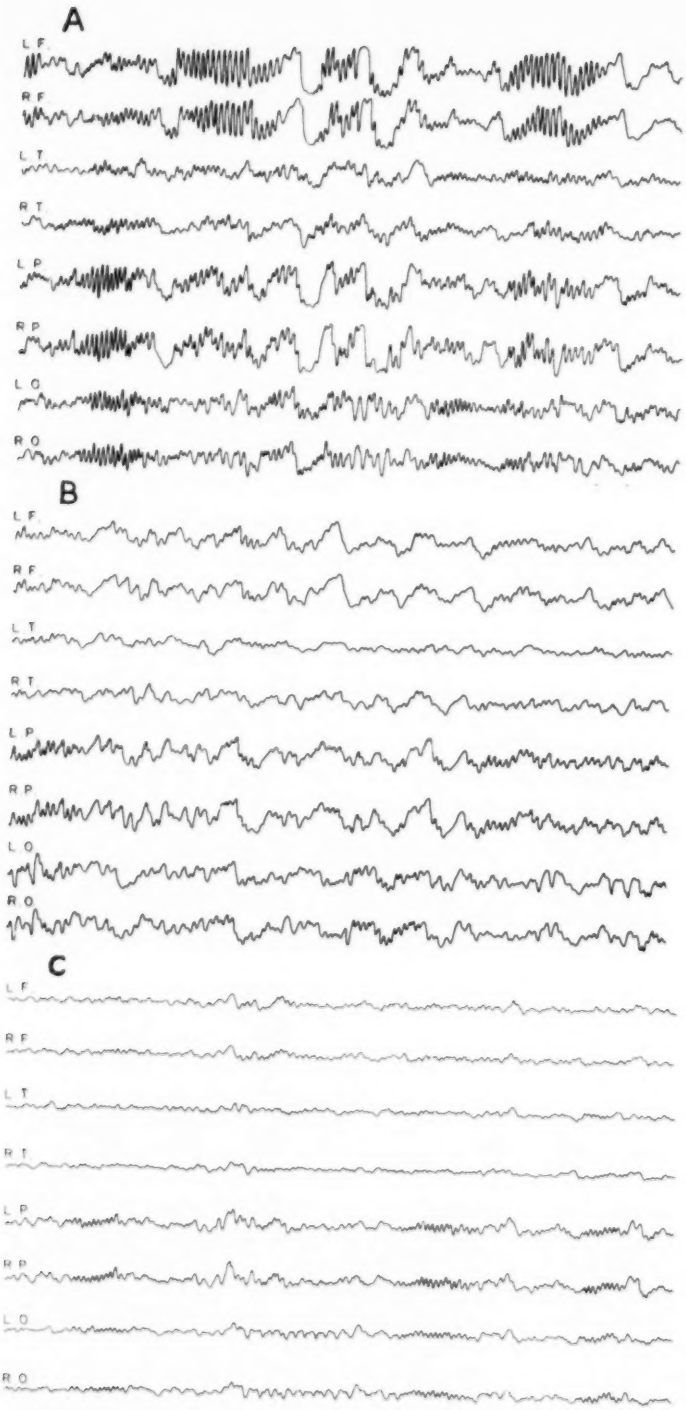

Fig. 3.—*A*, high-voltage sleep patterns; *B*, medium-voltage sleep patterns; *C*, low-voltage sleep patterns.

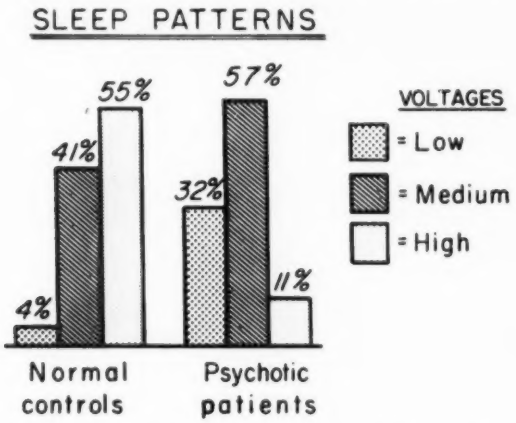

Fig. 4.—Sleep patterns in psychotic patients and in normal controls.

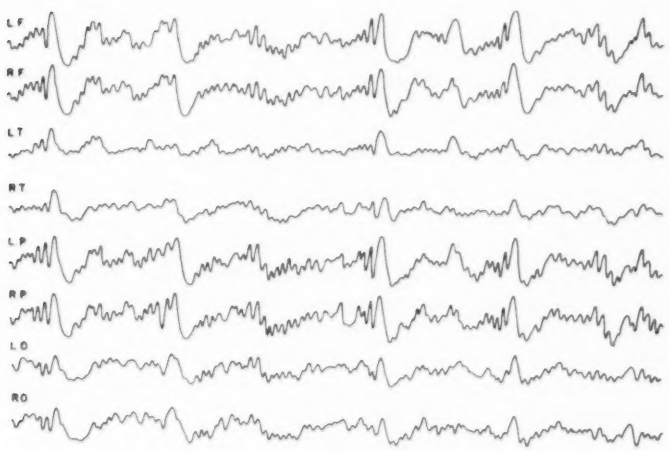

Fig. 5.—The mittens sleep pattern.

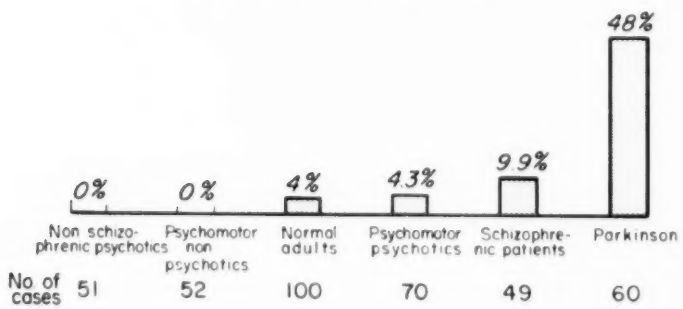

Fig. 6.—Incidence of the mittens sleep pattern in various clinical groups and subgroups of psychotic patients.

mitten patterns in various clinical groups and subgroups is shown in Figure 6. Among the small subgroup of schizophrenic patients, the mittens pattern occurred about one-fifth as often as among Leemhuis and Stamps' patients with Parkinsonism; however, it was twice as common as in the control group. No mittens pattern was found among the patients with nonschizophrenic psychoses, and none among patients with psychomotor epilepsy without psychosis. Therefore, this pattern cannot be considered generally characteristic of either epilepsy or psychosis. Among patients with a combination of psychomotor epilepsy and psychosis the incidence of the mittens pattern was the same as that among normal control subjects.

COMMENT

The present data indicate that patients with psychoses, when cleared of those with recognizable forms of epilepsy, do not have in their electroencephalograms a high incidence of borderline or cryptogenic abnormalities of the types seen in epilepsy. This statement holds for the electroencephalogram in both the waking and the sleeping state; thus, from the electroencephalographic evidence "pure" psychosis appears to be unrelated to epilepsy. Abnormal slow activity in the temporal lobe (a common finding in epilepsy) was not found in the present series, nor were other temporal lobe abnormalities observed.

The meaning of low-voltage sleep patterns is not clear. The only other condition in which the sleep pattern is reduced in amplitude is old age. With increasing age the amplitude of almost all sleep activity decreases.[1] Such highly developed patterns as 14-per-second spindles and biparietal humps, which are a common feature of the electroencephalogram recorded during sleep in youth, are relatively rare in old age; the sleep activity in the aged is characterized by poorly developed patterns.

Two patients, who were not included in the present series because they were arbitrarily selected on the basis of etiology, had a schizophreniform psychosis secondary to encephalitis; both had highly developed mitten patterns. The possible role of encephalitis as a cause of some forms of schizophrenia has been much debated. If mitten patterns can be shown to indicate disorder in the central gray structures, it might be possible by means of this criterion to separate from the total group of schizophrenic patients a subgroup with special etiological, physiological, and clinical features.

SUMMARY AND CONCLUSIONS

Electroencephalograms recorded during sleep on psychotic patients without recognized forms of epilepsy showed no evidence of epileptic disorder or slow-wave foci in the temporal lobes or elsewhere. The only significant findings were (1) a lower voltage of sleep patterns among the psychotic patients than among normal controls; (2) a higher incidence of abnormally fast activity among the schizophrenic patients than among other psychotic patients or in normal controls, and (3) a higher incidence of mitten patterns among schizophrenic patients than among normal controls, but a lower incidence than that reported by Leemhuis and Stamps [8] among patients with Parkinsonism.

Through the skilful assistance of Mr. Anton Engel, electroencephalographic technician at the Jacksonville State Hospital, it was possible to obtain artifact-free tracings during sleep on a most difficult group of patients, many of whom were combative and wildly hallucinating when they came to the laboratory.

Dr. Percival Bailey arranged the program for this research.

PSYCHODYNAMICS IN THE EXCESSIVE DRINKING OF ALCOHOL

JOHN W. HIGGINS, M.D.
NEW HAVEN, CONN.

AS FOR THE comprehension of illness in general, an understanding of the pathological use of alcohol calls for a synthesis of knowledge of the several biological and social sciences.

The particular contribution of psychiatry and psychiatrists has arisen out of experiences in the treatment of individual patients. Part of this contribution has been in the form of descriptions and classifications of different stages of intoxication with, and habituation to, alcohol. Allied to this, but more specially connected with interest in the psychotherapeutic approach to the problem of excessive drinking, has been the development of an understanding of the psychological forces motivating the impulse to drink excessively. An adequate review of the many ideas which have been proposed concerning the nature of these forces has previously been made by Bowman and Jellinek.[1] Consequently, it does not seem fruitful to estimate again the relative values of the various theories. Instead, the basis for the following discussion will be the psychoanalytic theory. This particular theory is chosen as the starting point for several reasons. First, and in general, although certainly not wholly explanatory, the concepts within it seem to offer a wider possibility of understanding the psychological motives in human behavior. Second, with reference to alcoholism particularly, certain of the psychoanalytic theories have already become extensively used, even among those who voice disagreement with them. Third, it formed the operational system guiding the clinical and dynamic diagnoses and therapeutic planning in the medical setting in which these patients were seen. Within this framework, the specific purpose of this paper is to present a hypothesis concerning the psychodynamics of pathological drinking which may serve to expand and modify certain of the current concepts about the problem.

The development of psychoanalytic ideas about alcoholism has itself gone through a number of stages, with changing areas of emphasis. For those who wish briefly to review these changes, there are available two extensive surveys of the

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Assistant Professor, Department of Psychiatry, Yale University School of Medicine.

This work was supported in large part by the Alcoholism Fund of the Public Health Federation of Cincinnati.

From the Departments of Psychiatry, University of Cincinnati College of Medicine and Yale University School of Medicine.

1. Bowman, K. M., and Jellinek, E. M.: Alcohol Addiction and Its Treatment, in Effects of Alcohol on the Individual, edited by E. M. Jellinek, New Haven, Conn., Yale University Press, 1942, Chap. 1, pp. 3-80.

literature by Crowley [2] and Lorand.[3] Although minor divergences of opinion have existed, there is an identifiable hypothesis which may now be regarded as the central one. Variations of it are widely accepted by psychiatrists working with alcoholic patients. The principle features of this dynamic reconstruction are best expressed in several papers by Rado [4] and Knight.[5] The impact of their papers is diminished when they are presented in summary fashion; however, since these dynamic concepts are basic to the discussion to be presented, précis of them should be given.

Rado's formulation of the psychopathological process of all drug addictions begins with the traditional psychoanalytic view of ego development. In the maturation of the ego, the boundless, omnipotent megalomania of the infant must be gradually modified through experience to a more modest self-evaluation. The narcissistic gratifications, originally obtained virtually effortlessly, must later be obtained through the individual's own coping with the environment, and his own achievements become the basis for healthy self-esteem. The development of the ego toward "realistic" adaptability may be impaired to such a degree by untoward life experiences as to make the individual uncertain that gratification can be earned in this way. Hence a longing is retained for the original, passively obtained, infantile megalomania. Later, in the face of real frustrations, there ensues what Rado calls a "tense depression." In this state, the individual is in a state of special susceptibility to a "pleasure effect" produced by a drug. When the need is great and the timing of the first experience with the drug is appropriate, this reaction of pleasure will be further reacted to with elation. This, he says, is the *sine qua non* for the actual beginning of the addictive process. The discovery is made that a self-administered "magical" substance can dispel the pain of reality, and in such a state of elation the boundless, original narcissistic state is reobtained.

Knight, in his more clinically oriented papers, has adapted this basic theory specifically to the problem of addiction to alcohol: He postulates the crucial infantile traumata as conditioning the individual to expect relief from discomfort by taking something into the mouth; the "discomfort" being assuaged arises out of excessive passive needs engendered by the parental attitudes. These needs are predestined to chronic disappointment and consequent rage. In this setting of inability to adjust to environmental forces a discovery is made: The psychic stress resulting from the inferiority feelings reactive to the passive oral needs is allayed by the use of alcohol, and the infantile euphoria is regained. Perhaps more significantly, the drinking can be regarded as a "socially condoned," and even praiseworthy, form of direct gratification by mouth.

2. Crowley, R. M.: Psychoanalytic Literature on Drug Addiction and Alcoholism, Psychoanalyt. Rev. **26**:39-54, 1939.

3. Survey of Psychoanalytic Literature on Problems of Alcohol: Bibliography, in Yearbook of Psychoanalysis, edited by Lorand, S., New York, International Universities Press, 1945, Vol. 1, pp. 359-365.

4. Rado, S.: Psychoanalysis of Pharmaco-Thymia (Drug Addiction), Psychoanalyt. Quart. **2**:1-23, 1943.

5. Knight, R. P.: Psychodynamics of Chronic Alcoholism, J. Nerv. & Ment. Dis. **86**:538-548, 1937; Dynamics and Treatment of Chronic Alcohol Addiction, Bull. Menninger Clin. **1**:233-250, 1937.

In essence, what has been stated in the theory, so far, is that a predisposed person with oral fixations is confronted with a difficult situation in life; the "difficult situation" means one which provides a threat to oral-dependent gratification. The threat may be related either to actual deprivation or to increased needs resulting from regression. The attempt is then made to alleviate the anxiety created by this situation by drinking, relief being offered through (1) the direct oral acting-out itself and (2) the state of euphoria (or "oral bliss") engendered by the intoxication.

It is this briefly summarized part of the theory concerning the inauguration of the addictive cycle that our suggested hypothesis tends to modify. On the other hand, our own observations have suggested no significant alteration in that part of the theory dealing with the events which occur in the midst of the addictive cycle. For discussion of this, reference is made to the original articles. The nuclear concept concerning the addictive phase, however, is that the excessive drinking itself gives rise to additional problems. In effect, the course becomes progressively downhill, consisting of cycles of alcohol-induced elation alternating with subsequent depression, which reinforces the need for more drinking. The process—disappointment—rage—hostile acts and wishes—guilt—masochism—increased oral and narcissistic need—becomes highly significant. The transitory elation brought on by the drugs serves mainly to renew the craving for their effect. The level of self-regard comes to be maintained artificially, and meaningful human relationships gradually lose their importance. They are replaced by the drug-induced pleasure. This implies a loss of the adult social and sexual contacts conducive to personality integration. Consequently, the disintegrative, masochistic tendencies become increasingly prominent. When, ultimately, drug-induced elation is no longer obtainable, a "crisis" occurs, which results in suicide, psychosis, or, in some instances, a disordered flight into an interval of sobriety.

The modification we suggest pertains mainly to the description by the writers previously cited of the series of events occurring before the actual onset of the addictive cycle. This sequence can be schematized as follows: threat of oral-narcissistic deprivation—anxiety (or "tense depression")—drinking—elation. The possibility of a modification of this view was suggested to us initially as evaluations were made of the early interview material of 52 new patients admitted to an outpatient alcoholism clinic at the Cincinnati General Hospital. For about one-fourth of these patients it did not seem that an emphasis on problems of orality offered the most reasonable way of understanding the psychic conflicts precipitating the excessive drinking. The interview material from a smaller number of patients who were undergoing psychotherapy also seemed to be in keeping with the possibility that a threat to the satisfaction of oral narcissistic needs is not always the primary initiating agent in the pathological use of alcohol.

On further consideration, such a possible modification seemed sustained by at least two other sets of factors. One concerns changes which affect the living situation of the problem drinker. There seems little room for doubt that, owing largely to the public relations work of Alcoholic Anonymous and other interested groups, the problem drinker recognizes his need for and seeks treatment earlier than formerly. As a result, therapists are not confronted with as large a number of patients who have already progressed into addiction. Consequently, some of the other psychodynamic factors may be a bit less clouded over by the narcissistic processes which seem specifically connected with the cyclical addictive phase. The same social

pressure may also contribute slightly to the drinker's decision to remain abstinent during treatment. Another, perhaps more significant, influence on the atmosphere of psychotherapy is the use of such a treatment adjunct as disulfiram (tetraethylthiuram disulfide; Antabuse). In many of the previously published papers on the psychological treatment of alcoholics, it is striking to see how many of the patients were confined to the hospital. How much such a therapeutic setting had to do with underscoring problems of dependency is difficult to say, but it might be expected to have been an influence in this direction. Also, if the patient was not hospitalized, it was apparently not infrequent that visits to the office were made either actually in a state of intoxication or shortly after a spree of excessive drinking. In such conditions of toxicity, the resulting psychological impairment would significantly influence the behavior and interview material of the patient. There is some evidence to suggest that this influence would be in the direction of emphasizing ego pathology and narcissistic problems. In a large number of cases, as a result of the social influences and of the use of disulfiram we are enabled to see office patients as they continue to live their ordinary, but sober, lives uncomplicated by these added factors. (The new problem of the psychological meaning of disulfiram is one yet to be explored fully.) In summary, the fact bears reemphasizing that in approaching the problem of "chronic alcoholism," one should not, for various reasons, confine one's thinking to actual alcohol addiction.

The second set of factors contributing to a modification in theory is connected with the reshaping of views about the action of toxic substances on personality functioning. A steady advance is taking place in the breadth and depth of concepts in the field of psychopharmacology. On the one hand, research in this field indicates that there are predictable qualitative differences in the psychic effects of such agents as the opiates, alcohol, barbiturates, and marijuana. All these are substances to which addiction or habituation occur. The implication is that a theory explaining the pathological use of one of them must include careful consideration of the substance used and the specific pharmacological action to be expected. On the other hand, and perhaps more pertinent to the subject, evidence continues to be accumulated that in the same patient, the same drug is capable of producing divergent effects, depending on the dosage and, more importantly, on the patient's psychic state at the time the drug is taken. Emphasis has been placed on the tenet that the psychic effects of a toxic substance can be fully comprehended only if the immediately pretoxic psychic state is also understood. The theoretical construct for the latter idea has been beautifully presented in an original and stimulating, but neglected, paper by Gross.[6] For further evidence supporting these psychopharmacological concepts and a review of the logic in their formulation, reference is made to the more recent papers by Lindemann and Clarke[7] and Wikler.[8]

These concepts seem to us to coincide with the theoretical modification we suggest. They imply a certain diversity of expected effects from the use of alcohol as an intoxicant. Such variation can actually be observed in the immediate and long-range

6. Gross, A.: Psychic Effects of Toxic and Toxoid Substances, Internat. J. Psycho-Analysis **16**:425-438, 1933.

7. Lindemann, E., and Clarke, L. D.: Modifications in Ego Structure and Personality Reactions Under Influence of Effects of Drugs, Am. J. Psychiat. **108**:561-567, 1952.

8. Wikler, A.: Mechanisms of Action of Drugs That Modify Personality Function, Am. J. Psychiat. **108**:590-599, 1952.

behavior of chronic, excessive drinkers. To explain this, it appears necessary to reexamine the possibility of a diversity of pretoxic psychological determinants.

In order that this discussion may remain within the proper boundaries, however, certain common denominators in the problem of chronic alcoholism should be acknowledged. First, the substance used is always, obviously, alcohol; second, it is always taken by mouth. We are prepared to suggest that the latter may not always be of great importance. The first, the fact of a drug with specific pharmacological action, cannot be evaded. Alcohol is recognized as a depressant of the central nervous system. The significant question is this: To what use is this action put? In what way does it come to serve as a defense against anxiety? First, it might be contended that a kind of direct action occurs; the narcotizing effect diminishes awareness of anxiety, or of the anxiety-provoking situation. Earlier, the concept was reviewed which holds that this anxiety arises out of conflict about oral narcissistic gratification. The first suggestion of this paper is that further attention be directed to the idea that the anxiety of which awareness is being thus diminished does not always have to do with this specific conflict; it may also arise out of conflict over sadistic, genital-sexual, or other impulses; or the anxiety may concern the activation of psychological defense mechanisms against such impulses.

The second suggestion is related to the first: Through its depressant action, the alcohol may have its principal function in facilitating the operation of a psychic defense mechanism. Such a defense mechanism may not necessarily be connected with oral conflict. For example, the depressant action of the drug may be put primarily in the service of character defenses involved with conflicts about adult sexuality, such as pseudogenital "acting-out," or even in the development of a protective symptom, such as a hysterical dissociation.

In short, then, a revised hypothesis can be briefly expressed in the following way: A predisposed person (and the predisposition may represent fixations at various levels of personality development) is confronted with a difficult life situation; the "difficult situation" may or may not be one which has as its primary component an "oral threat"; an attempt is made, through drinking, to handle the anxiety aroused by this conflict. The drinking may serve as a defense through various channels; it may bring diminished awareness of internal or external stress, or it may facilitate defenses previously inhibited.

Several case histories are presented to show the kind of data which gave rise to this hypothesis. One case is reported in a moderately lengthy fashion; the others, in the form of vignettes. The longer case report demonstrates the material more fully and illustrates our use of it. All the therapy sessions were conducted in face-to-face fashion. This technique may have resulted in some blocking of the verbalization of oral material. However, the evidence available in the cases being presented seemed coherent and consistent enough to justify the conclusions drawn from it, supporting a hypothesis which does not rest on oral frustration as the keystone.

CASE 1.—This is the history of a 50-year-old man whose drinking played a significant role principally in the conflictual area concerning his hostile aggressive impulses toward and fear of women. The information was accumulated during the first nine months of weekly interviews. One of the initially striking features about his case was the contrast between the promise he showed in his early life and an apparently repetitive pattern of self-thwarting, resulting in his state of degradation on his coming to the clinic. Before the onset of his alcoholic problem he had been a successful writer. At the time of his application for therapy, he had been living an almost marginal existence at a Salvation Army home for several years. His physical

appearance itself dramatized his lowered situation. His unattractive appearance was accentuated by his choice of ill-fitting, unkempt clothing, slumped posture, and a fatuous, toothless smile. In contrast, his use of language evidenced a highly developed cleverness and intelligence.

His excessive drinking dated back more than 20 years. Although there were variations, the typical pattern he followed was to drink small amounts almost daily in bars, which amounted to no more than a pint (500 cc.), reaching recognizable drunkenness about two or three times a week; on week ends, or in time of special distress, he would buy several "fifths" of whisky, retire to a room, and drink until they were gone, passing in and out of coma.

Past History.—The patient and his brother, four years older, were born to upper-middle-class parents in an industrial city. The family setting of his early rearing included his parents, brother, and maternal grandmother. In the childhood years there was apparently some competition between him and the brother for better scholastic and physical performance; however, with the passage of years, they drifted apart and have had little meaningful relationship since except for the older brother's giving "handouts" in time of need. Throughout his childhood the patient was regarded as being "sickly and weak." The more significant experiences involved the interplay among his mother, grandmother, father and himself. His father died when the patient was 9 years old. Before that time the father had been a moderately successful physician. Although he was held in high regard by the community, he was personally a meek, submissive person, wholly under the sway of his wife and mother-in-law. Periodically, the father would retreat to his room or to another city and drink large quantities of liquor. Occasionally, he would use morphine in the same way. In retrospect, the patient believed that these episodes were the only times in which the father expressed his individuality. Because the father was widely regarded as a person of great dignity and refinement, the sight of whisky bottles in the family trash was interpreted by the neighbors as meaning that the mother was a dipsomaniac. In contrast to the father, the mother and grandmother were determined, ambitious, and dictatorial in their attitudes.

From this childhood experience with his father, he learned to distrust an outward appearance of success in men. In his father, he had come to see that this overlay a "weak," submissive attitude. His further interpretation of this was that the women in his family, by their controlling and aggressive attitude, were the agents of the father's weakness. The only show of "masculinity" he recognized was the rebellious, self-destructive drinking.

In his relationship with his mother, he spoke of her possessiveness as "a mother lion with her cubs." An area in which he especially experienced her influence concerned sexuality. He complied so completely with her restrictions that through his adolescence usually he was not even aware of sexual impulses toward women. Instead, he practiced masturbation, with the fantasy of himself being spanked by a woman. In the interview in which this practice was first discussed, his remarks about it recalled to him an incident which occurred around the age of 4 or 5 years. He remembered that he had been playing with a little girl who hit him, "or did something of an aggressive nature," and that her mother, upon seeing this, came out and spanked her. He "supposed" that he must have "identified" himself with her and that this act was somehow "homosexual." In the interview, the sequence of thoughts following this concerned his impotence in the first week of his marriage, his past thoughts that masturbation led to impotence, and a question about himself being "so much a feminine person that [he] disliked aggressiveness and pugnaciousness." In other respects, in his childhood relationship with his mother, his reaction to her imperiousness was to adopt an attitude of submissiveness, and his surface behavior came to approximate the meek and passive one of his father. In general, his life was oriented toward pleasing his mother, out of fear of her. For example, from an early age he was rather precocious intellectually. His performance in this area could have become a way of fostering his own self-recognition. Instead, because of the premium she placed on it, the attaining of intellectual success soon became a way of expressing his compliance to his mother. A fear of failing was one of his two prominent childhood fears; the other was of being punished for something unknown. Concerning these fears, he recalled an incident in the first grade when he was sent to the principal's office. Expecting punishment for something, he was simply notified that he was to be advanced to the second grade, "just because" as he said, "I could spell Mama and Papa." As he continued his schooling, through the university years, he did well scholastically and in later years showed especial proficiency in creative writing.

After a several years' courtship, he eventually married. His choice of a wife was in keeping with the trends developed in his relationship with his mother. His wife was a domineering woman, to whom he had been first attracted on the basis of similar intellectual interests. He commented that during the courtship he "wasn't aware of anything below the waist." Two children were born of this marriage.

Setting of the Onset of the Problem Drinking.—After graduation from college, he had progressed in the writing field. In the late 1920's he entered the field of magazine editorial writing. About the time of the birth of his second child, a son, he was just beginning to achieve real status in his profession and was receiving recognition for it. He had moved to a metropolis and felt that he had attained significant success, with prospects of doing better. With this, he became intimately associated with a sophisticated social group, in which fairly free license was given to sexual activity. At the same time, his wife was growing less openly praising of his intellectual exploits and work progress, and she was voicing dissatisfaction with his sexual performance. About the latter he was especially resentful, saying that she expected him to be an "athlete."

This combination of circumstances constituted a threat to his usual pattern of adjustment. The birth of his son probably constituted a threat to dependency gratification. Beyond this, however, the momentum of his own achievements was carrying him beyond the ordinary result: It was releasing him from the control of the mother surrogate, and identification with the impotent father was becoming less tenable. What seemed to happen was that he was brought to, or near to, awareness of the gap between his pseudo-phallic-intellectual defense and his feelings of genital inadequacy. He had several reactions to these events. One was open hostility to his wife, which he rationalized on the basis of her being a "phony" intellectual. It was in this setting that he began to drink heavily and, with this, to philander and to begin effecting a separation from her. In the course of several months, he became a full-fledged bohemian, drinking heavily, and having transient sexual affairs. In this situation, the drinking can be understood in a general way as an identification with his father's thwarted masculine protest. As a second reaction to his feelings of genital inadequacy, there occurred a good deal of sexual acting-out. Previously, such activity was blocked by fear of and hostility toward women as castrating figures. This block was partially overcome via the façade created by the rebelliousness of the drinking. In addition, awareness of the expected anxiety in the specific heterosexual contacts was reduced through the intoxication. Thus, the drinking can be interpreted as serving largely as a defense against castration anxiety. In addition, it cannot be gainsaid that the drinking is also understandable partly as a substitute for the oral gratification previously obtained in a dependent relationship with a woman.

Several months after the separation from his wife, he began to live with, and form a closer bond with, one particular woman. She was a highly intellectual, aggressive, sexually active person. He thought of her as a "strong" woman. In her attitude toward him, she offered recognition of both his intellectual and his sexual prowess. It gave him a feeling of "being masculine" and of strength to be gruff and inconsiderate with her when he was drinking. When he was with her, the drinking served the same functions as those already mentioned, with special facilitation of his pseudomasculine sexual behavior. During the course of this affair, he wrote his most widely read and successful article. However, shortly after, his adherence to work was so irregular and marred by his drinking that he was fired. His opinion was that the managing editor was "scared" of him; that is, he was concerned lest he be overcome by the patient's progress. This event marked an acceleration of his social and intellectual decline. It was one of the first real attacks on his phallic-intellectual defense. His subsequent writing, strongly influenced by the left-wing interests of his paramour, was increasingly poorly received. His cavalier attitude toward her and his drinking became more intense. Despite this, he was not then, or later, aware of any hostility toward her. However, when she suddenly died of an acute illness, he felt that his unseemly behavior had contributed to her death. On this basis, it can be postulated that the drinking itself was a means for the expression of his hostility.

After her death, he drank steadily for a month, finally requiring hospitalization. The drinking at that time is understandable as being in part a continuing expression of hostility to her, and in part, via the intoxication, as a means of diminishing the awareness of his guilt and depression. However, this also marked the actual beginning of the addictive phase of his drinking, and the needs being satisfied by it were by this time also products of the drinking itself.

This episode was the beginning of more than a decade of addictive drinking, with increasingly poor work and social performance, culminating in his status when he appeared at the clinic. The (to him) "phony" defense of intellectual achievement was virtually abandoned and gave way to the "true" masculine activity of drinking. Even minor successes in jobs became the signal for getting drunk. For example, one of his jobs was writing speeches for executives of a business concern. It was his attitude that the company was "stupid" in letting him miss time during hangovers. He finally became most dissatisfied with his own performance, went on an extended drinking spell, and was fired.

In the intervening years, he made several passing attempts at relationships with women. These episodes were fairly uniform in variety and in keeping with his statement of admiring "strong" women. The usual thing was for an ambitious, controlling woman to become interested in his literary ability. She would then attempt to "rehabilitate" him. Ordinarily, he would assume the role of being protected and make feeble gestures at writing. These quickly revived the old mother-son conflicts and were forthwith broken. He would shortly resume drinking and discard the woman as being "stupid" or "domineering." It is interesting to speculate about the one possible continuing expression of the old mother-son relationship. He had always identified organized religion with his mother. In recent years, his means of staying alive was his attachment to the Salvation Army. He managed to please the officials of this group by his adeptness in writing an institution newspaper. Their praise of him would eventually make him uncomfortable, and he would drink.

One of the sequences in therapy, although shedding no specific light on the drinking itself, illustrates something of his way of meeting situations which arouse conflicts related to those in which drinking does play a role. In one interview, having mentioned being enuretic after drinking, he recalled a dream "about getting drunk." In it, he was in a restaurant and a major of the Salvation Army was sitting there, reading a newspaper, and did not notice the patient. In turn, the patient saw that "the Major had no head at all. He was in a Salvation Army uniform, but it was not an exact outfit." The patient was annoyed in the dream because the other could not talk to him, and he felt "anxious and lost." The man in the dream was a person much admired by the patient because of his drive and ambition. However, the patient saw him as basically weak because of his connection with the church. After this dream, he related a fund of information about his childhood, especially as it pertained to his father. One repetitive thought he expressed about himself concerned his "surprise" at the discovery of the pleasure to be had from money, drink, and women. When this thought was pointed out to him and doubt was expressed about it, he entered a flurry of intellectualization, but ended by describing his masturbatory fantasy of being spanked by a woman. In the following interview, he brought in drawings he had made to stimulate this fantasy and discuss it further. In effect, he asked the therapist to tell him whether or not this meant he was homosexual. When his request for a specific reply was refused, the patient first became highly adulatory of what a good doctor the psychiatrist was. In turn, the therapist pointed out his oversolicitude as a means of handling anxiety, reminded him of his past statements about disliking all men and liking all women, and suggested that these involved his homosexual fears. The patient's response was to say, "You do have big, brown eyes." When it was indicated to him that this remark was in keeping with the previous interpretation, the patient became exceedingly anxious and hostile and left the office.

A fairly specific constellation of personality dynamisms has been traced in the development of an understanding of the origin and purposes of the symptom of excessive drinking in this man. In pursuing the path of such development, it is not intended to imply that a complete analysis of his personality working has been gained; rather, the focus has been on those areas of conflict into which drinking was significantly introduced as an attempt at solution. One of the products of his early life experiences was that women (in the person of his mother) were to be regarded as powerful and potentially destructive of man's strength. In the person of his father, he saw such a weakened man whose main expression of "masculinity" and hostility toward women was defiant drinking. The patient's reaction was to adopt an attitude

of passivity to and dependence on his mother. His intellectual prowess, a potential source of strength, became instead a means of fostering this relationship and a means of handling his fears of women. At a particular period in his life, the equilibrium of these forces was upset. The birth of a second child threatened the protected relationship with his wife; the defensive function of his intellectual prowess was losing its effectiveness. With this, he was threatened with awareness of his feelings of genital inadequacy. The function of the drinking in this situation is discussed, the drinking serving as an identification with his father's pseudomasculine drinking, as an expression of hostility to his wife, as a means of facilitating the defensive sexual acting-out by diminishing awareness of the anxiety connected with it, and as a substitute for the oral gratification previously obtained in his relationship with his wife. During the subsequent affair with his paramour, the drinking served many of the same functions. The drinking at the time of her death is understandable as a defense against the awareness of his hostility to her and his guilt connected with this. In addition, at a deeper level, it probably represented an attempt to destroy his introjected image of her.

There follow several greatly abbreviated case histories, which purport only to offer further illustrations of some of the psychic mechanisms in the service of which pathological drinking can function. The sequence of their presentation is such that the significance of nonoral factors diminishes with the successive cases. For example, they are of major importance in the first two cases whereas in the last case the oral narcissistic elements predominate.

CASE 2.—A divorced woman aged 34 requested treatment for her drinking problem when she became alarmed at her behavior during "blackouts." Examination of the circumstances of her excessive drinking revealed them to be involved with her confused relationships with men. This area of conflict, in turn, stemmed largely from her early experiences with her parents. Her own father had deserted when she was about one year of age, and her mother had remarried about a year later. During childhood, she and her stepfather were very close; by the time she reached adolescence, their relationship was the intimate one of man and wife except that there was never any sexual activity. Although she never saw her own father, the knowledge of his existence seemed to make it "safe" and agreeable for her to continue in the relationship with her stepfather. In late adolescence, when she learned of her own father's death, she became less close to her stepfather. With the passage of time, her usual attitude toward all men was to be exceedingly rivalrous with them in business, and in her personal contacts to assume an air of humorous sophistication, which thinly veiled her tendency to demean, attack, and manipulate them. When she eventually married, it was to a man she knew to be a weak, unsuccessful person. For the first six or seven years of marriage she dominated the household, often threatening to divorce him. At the end of that time, his attitude somehow changed, and, among other things, he became highly successful in business. Within a short time he abruptly divorced her. This event dealt a significant blow to a pattern of adjustment which she had considered stable. It was at this point that her periodic spree-drinking began. In general, her subsequent attempts at linkages with men were failures. Usually, either she selected apparently stable and strong-willed men who were already married, or she picked weak or neurotic (and, twice, psychotic) men who were too obviously poor prospects for permanent companionship. The drinking came to be utilized in the "solving" of the conflicts in these associations. On several occasions she came in contact with men whom she could reasonably hope to attract and marry. Each time that the affair neared culmination, either in sexual intercourse or in a proposal of marriage, she would become drunk and make vicious verbal attacks on the man. At the same time, the episode would have the effect of debasing her. The "blackouts" began to occur when, after some years of living alone, she moved back to the parental home. Here, she made a fairly unsuccessful attempt to revive her former intimacy with her stepfather. The principal results were an increase in her feelings of frustration and a resurgence of hostility to her mother as a

rival. She began going to social gatherings, where she would drink heavily and behave flirtatiously with the men. When the situation would become too heavily charged with sexual feelings, she would suffer a "blackout"; during this, she would partially or wholly disrobe or make coarse sexual advances. Occasionally, these advances amounted to actual physical assaults.

CASE 3.—The initial application to the clinic of a 36-year-old, divorced, semiskilled laborer was largely in response to the demands of his employers. His periodic alcoholic sprees had brought his job into jeopardy. However, he had also come himself to see that drinking constituted a problem. Although he had made previous resolutions, once he took a single drink, he felt he had "broken a pledge" and went on to complete intoxication. Having begun to drink, he would, during the past seven years, go on sprees of daily drinking, lasting for several weeks or several months. His own thought was that "seeing [and becoming attracted to] a pretty woman" had something to do with his getting him started. His history further bore out this thought that a major function of his drinking was a part of a defense system against anxiety connected with heterosexual impulses. From childhood, his usual surface behavior had been marked by diffidence and shyness. This attitude was abetted by the authoritarian and restrictive attitudes of both his parents. The main outlets for his aggressive impulses were usually devious: In childhood, he had repetitive dreams of "firing a boiler," "driving a trolley," and "shooting people." During adolescence, he often provoked arguments with his father about religion and politics, usually turning out the loser. During the years of early adulthood, he found that he could, with the aid of alcohol, be as much of a roustabout as his contemporaries. During this period he had a number of brief sexual contacts, always when drunk, and with women of poor reputation. Eventually, he was attracted to his future wife by her beauty but was unable to bring himself to talk with her. One day he became drunk and not only talked with her but tried to force sexual relations. This resulted in a scandal in his small town, and she agreed to marry him. His wife turned out to be frigid, blamed him for her lack of satisfaction, and began to consort with other men. His response was occasionally to philander, but only if intoxicated. This propensity of his was greatly strengthened when, after having "confessed" to her as a gesture of boasting and defiance, she scoffed at him and doubted that he had done so. About the same time he contracted gonorrhea. He said that it was in this period that he "began to lose the pleasure of drink," by which he mean that he began to drink excessively. Eventually, he and his wife were divorced, and he continued his philandering. The "long sprees" seemed to coincide in time with the periods of his having affairs. One such affair was attempted after the beginning of treatment. Shortly after meeting the woman, he began to drink again and interrupted his clinic visits for two and a half months. When he finally returned, he was intoxicated. At first, he related the details of the affair with a boastful attitude about his sexual powers. After the giving of this part of his story, his demeanor changed, and he anxiously asked why the therapist looked so angry and expressed the fear that the physician was going to "hit" him, or perhaps "murder" him. His whole attitude then became one of abject compliance.

CASE 4.—A 43-year-old married woman asked for help in overcoming her spree-drinking, of four years' duration. Periodically, she had been becoming drunk for from one to several days. These episodes occurred from once every four or five weeks to twice a week. The onset of this problem was clearly related in time to her husband's having had a myocardial infarction. Up to that point, the marriage had served to hold in balance neurotic needs stemming from childhood experience. She had been born out of wedlock; although her parents later married, she was never a permanent member of the household but was raised instead by her maternal grandmother. Her interpretation of her parent's attitude, furthered by the comments of the grandmother, was that it was due to her being the result of an "immoral" union. Her shame about this, coupled with her guilt about several adolescent sexual experiences, led her to adopt a defensive aloofness from sexual matters. When she eventually married, it was with the predominant conscious attitude that this was a means toward obtaining security. Barely tolerant of her husband's sexual advances, she was not displeased when he formed the custom of going regularly to prostitutes for his main sexual outlet. With this arrangement, she settled fairly comfortably into her role of the person who oversaw his welfare and to whom he could confide and look for advice in business matters. Whenever he did insist on intercourse with her, she was able to allow this mainly as a "favor" and in keeping with her basically dependent attachment to him. However, about a year before his heart attack, he had volunteered to give exten-

sive financial help to her sisters. She had always resented these siblings but had not dealt with them for almost 20 years. This step of his put them into the role of rivals for her husband's protection. This threat, plus the concern aroused by his critical illness, had weakened the dependent security of her marriage. While she was nursing him through his acute illness, she felt closer to him than usual. After his convalescence, on the advice of his physician, he discontinued his philandering and looked to her exclusively for sexual partnership. Because of his own personality, he no longer acted toward her as his confidante. Unable to interpret her role with him as the safely dependent one, as previously, she reacted with anxiety to the frank sexual relationship. For the most part, this was expressed as strong hostility to her husband. Drinking gradually became useful in this situation. At first, she found that if she was slightly intoxicated she "did not mind" intercourse. Then she found that if she became drunk enough her husband would not approach her. In time, an overture by him became the signal for several days of excessive drinking. When a physician pointed out to her that her drinking was expressive of hostility to her husband, the statement served mainly to intensify the sprees. In short, the drinking became part of her expression of hostility and, with the subsequent intoxication, served to diminish awareness of sexual anxiety. The alcoholism can also be interpreted as being a partial substitution for the dependency gratification previously received in the relationship with her husband.

CASE 5.—A 48-year-old married salesman initially sought treatment for his excessive drinking at the behest of his wife. He had for some years been in the custom of drinking about 10 oz. (300 cc.) of whisky a day, with periodic sprees of increased drinking. This had had the recent effect of greatly diminishing his productivity as a salesman, and he viewed himself as a "magnificent failure." On review, his alcoholism seemed to be involved with his conflict about attaining success. Until he married, in his early 30's the patient had lived with his parents in a farm area. His father had inherited a fair amount of money and presented himself as a "country squire." Actually, he was an unsuccessful, wasteful person, who was almost poor when he died. The mother was thrifty and hard-working. Neither parent manifested particular interest in the patient or his brother, three years younger, except in the comparison of their relative accomplishments in school or sports. In an early interview, the patient related a dream which led him to comment on certain childhood experiences. The dream was of "two living objects, one of which was necessary to the other, and yet on a slave basis. The smaller was able to overcome the predominant characteristics of the larger." This dream had led him to discuss various situations in his life in which he had fallen just short of success—in school, in music, in teaching, and in his jobs. From this, he went to a discussion of his past practice of coitus interruptus, and thence to a recollection of his "disappointment" when, as a child, he first discovered that a girl did not have a penis. He also recalled that about the same time he had gone with his father to the city for treatment of a bleeding, infected navel.

As an adult, the patient's surface attitude was one of great dignity and reserve. In sports and games, as well as in business, he voiced much determination to beat out others. He rationalized his actual lack of success as "bad luck." His tendency to drink excessively began in time relation to two events: One was the birth of his son; the other was a signal failure in a previously comfortable business arrangement. In the latter, he had passively achieved some success by attaching himself to his father-in-law who directed the company. The patient's wife reported to a case worker that as their son was growing up the patient was always extremely competitive toward him, placing great emphasis on a need to beat him out. At the same time, he seemed to obtain vicarious enjoyment out of the son's intellectual progress through school and university. Although indulging in periodic sprees, his over-all performance in his own work was at least satisfactory. This changed, however, with the son's graduation from professional school and marriage. His drinking became heavier and daily. The son's superseding him in this way seemed too great a blow, and he virtually abandoned his previous competitiveness. The presumptive interpretation is reasonable that anxiety arising out of the competive hostility to his son was bound by the alcohol intoxication. Drinking, in its general effect, was the steppingstone to a reduction in his stature at home and at work. In business activity, exacerbations of his drinking occurred when he was confronted with the probability or fact of succeeding in a particular venture.

Case 6.—In this case, although, again, there is a mixture of factors influencing the excessive drinking, the most dominant concern frustration of oral narcissistic needs. A 32-year-old man, at the time of his asking for help from the clinic, had been an excessive drinker for 10 years and a daily drinker for 7 years. Although he managed to remain employed as a salesman, the actual source of financial support for him and his family was his father. The patient was the youngest of six children of a well-to-do and socially prominent family. His father was an exceedingly aggressive, successful man. His usual position in the home was characterized by a remoteness, which he justified on the basis of his being "too busy." He ordinarily executed his parental responsibility by providing ample money to his wife and children. However, occasionally this attitude was transformed into one of judging his children harshly and demanding excellent performance by them. If they failed in some endeavor, he adopted the technique of teasing and criticizing them bitterly. From the time of his later childhood through to the present, the patient's reaction to these verbal attacks was to maintain a bland facade and, as he said once, to "swallow (his) feelings." His relationship with his mother contributed to this pattern. She was excessively protective and indulgent of his wants. He could never recall her frustrating his wishes for anything. From childhood, if he wanted something, he would forthwith buy it on his parents' account. In addition, he always made use freely of his family's prominent name to gain favors in school, jobs, etc. A personality characteristic correlative to this was his high optimism. He never voiced any doubts about his ability to excel, despite repeated failures. Even when, in later years, he literally did not have sufficient money to buy food for his family, he would make extravagant purchases to satisfy a personal whim and expect that "somehow" the bill would be paid. In fact it was—by his father, who was interested in protecting the family "name."

The patient's early drinking seemed, in retrospect, largely a gesture of defiance against his father and a component of a flimsy pseudomasculine façade. In later years, however, the dominant factor was not this. The exacerbations of his drinking usually occurred in direct reaction to such events as the birth of his children. Although he ordinarily verbalized fondness for them, his major feeling was one of resentment for the responsibility they put upon him. Even more pointedly, his drinking appeared when his overly optimistic self-regard was disturbed. If his fantasy of being an outstanding, successful businessman became untenable because of a defeat, or because realistic demands were made on him to produce, he would become drunk. When possible, he would drink in a fashionable place, conversing urbanely with men he regarded as successful. Whether or not he could arrange this, he would go on to intoxication, which seemed to serve mainly as a means of withdrawal from the demands of reality to a state of blissful, objectless self-satisfaction.

In the several months in which he remained under therapy, he maintained an attitude of aloof good humor and condescending politeness, with the result that he never allowed the development of a meaningful human relationship with his therapist.

One last case is outlined briefly to depict a kind of end-point in the scale of dynamic patterns in alcoholism which are illustrated in this series. It provides a contrast especially to the first of these vignettes. It is selected because the predominant mechanism of the drinking was so directly stated by the patient himself.

Case 7.—A 39-year-old man was strongly urged by the Court of Domestic Relations to consult the clinic concerning his alcoholism. Because he considered his drinking as a "habit" which he "did not need," he consented. His excessive drinking began when he was overseas with the Army in World War II. He linked the onset directly in time and in reaction to his being notified of his mother's death. He explained, "Drinking makes you forget—until you're over the drink, and then you feel worse; so you start again." On his discharge from the Army, he married a feebleminded woman, and, being of a submarginal income group, they moved into a slum area. Three children were born in rapid succession. He spoke glumly of his bad housing, sickly children, "stupid" wife, and "bad neighbors." He showed a marked tendency to view all his life difficulties as the result of other people's faults. He made the discovery that he could "forget" his discomfort about all these things through drinking. He likened his "habit" to a "baby with a pacifier—you have a baby who's crying, and you put one of them in his mouth; he stops crying. That's the way it is with drink."

The patient himself was the 16th of 17 children, the father of whom deserted when the patient was 3 months old. Despite having seen his father only twice in his life since, he denied any resentful feelings toward him, saying, "You're supposed to love your parents."

It would seem that the predominant psychic mechanism in this man's drinking was the attempt to gratify oral narcissistic needs and to ward off the anxiety resulting from the frustration of such needs.

CONCLUSION

It must be admitted that to date no clear and wholly convincing theory is available to explain the specific "choice" of excessive drinking as a defense against anxiety. The evidence for and against hereditary and physiochemical factors is still too meager to permit an adequate judgment as to the significance of either. Certainly, the role of various cultural influences is an important one, but the weight of them and their particular means of operation are in only an early phase of investigation.

This paper has been concerned with a reexamination of the factors operating specifically within the psychological sphere. As for most symptoms of psychic illness, it can be said that the symptom of excessive drinking is determined by many factors. This, of course, need never preclude the search for the most significant ones. Concerning psychological factors, there are various theories, but the most pervasive of these conceives the predominant force in excessive drinking to be the gratification of oral narcissistic needs and the alleviation of the anxiety produced by the frustration of such needs. Despite the wide applicability of this concept, our conclusions have not been in total agreement with it.

Our observations indicate that when attention is focused on the circumstances early in the course of the illness such a restricted dynamic theory is not tenable. Rather, it appears that drinking and intoxication can be put in the service of defense mechanisms against various sources of anxiety: The depressant effect of the alcohol may simply reduce awareness of anxiety; or the act of drinking, together with the pharmacological action, can facilitate the expression of other previously inhibited psychic defense mechanisms. Our case material does not support a generalization that the immediate source of the anxiety is related to oral conflict. Instead, the nature of the anxiety being assuaged by drinking appears to vary from one drinker to another. Yet a synthesis of these apparently divergent theories seems not only possible, but indicated. In order to effect this, the clinical course of chronic alcoholism is conceptualized as a continuum of varying degrees of severity. The estimate of any patient as having "mild" or "severe" alcoholism ordinarily comprises an evaluation of how much of his total behavior represents conformity to the reality situation and the maintenance of mature object relationship and how much of his life is centered around satisfying the craving to drink. To understand the forces deciding where on this scale between "mild" and "severe" the alcoholism of a given patient will be, the following hypothesis is suggested: On the basis already discussed, drinking may arise out of a variety of psychological conflicts. The individual episodes of inebriation may or may not be severe, probably depending on the intensity of the anxiety and the person's ability to form other defenses. Whether or not drinking persists or becomes repetitious probably depends initially on the continuation of the conflict situation. As the episodes of intoxication continue, they themselves begin to become contributory to the appearance of subsequent episodes, as is fully discussed in the introductory paragraph of this paper. For example, a person may begin to drink excessively mainly to assuage anxiety about heterosexual conflicts. Problems

pertaining especially to oral narcissism initially may be minimal, or possibly absent. As the drinking episodes become more frequent, at times the "pleasure" obtained from the intoxication may begin to supersede as a goal the relief from the original stimulus—anxiety. As the process continues, the original psychodynamic conflict becomes overshadowed by the "nonspecific" oral narcissistic elements. This could explain the heterogeneity in the psychodynamics of "early" alcoholism and the dominance of the more primitive oral narcissistic elements in "severe" alcoholism. As corollary of this hypothesis, if the individual psychodynamic conflict concerns gratification of oral narcissistic needs, the more malignant is the course of the illness likely to be. In summary, it might be said that the nature of the anxiety being assuaged by pathological drinking may vary not only from individual to individual, but also within the same patient, depending on the "stage" of the illness process.

This revised formulation, obviously, has implications for psychotherapeutic attitudes. If the theory is correct, it would bespeak more flexibility in the evaluation of the needs of alcoholic persons. A therapy projected on the assumption that oral narcissistic needs are paramount could be incorrect. At best, the therapy may be ineffective; more importantly, regression may be fostered at a time when a more direct, aggressive therapeutic approach would be opportune.

The ideas expressed here require further checking by the examination of a larger mass of case material, and especially of the more intimate detailed information of patients in definitive psychotherapy.

SUMMARY

In the present state of knowledge, it would appear that the symptom of excessive drinking of alcohol and addiction to alcohol are the products of various social and biological forces. This paper is concerned predominantly with a scrutiny of the individual psychological factors. For specific reasons, the particular framework of the theoretical discussion is that generally outlined by psychoanalytic theory. In the introductory section, the most widely applied psychodynamic hypothesis is summarized. In brief, this emphasizes the importance of oral drives in the motivation to drink excessively. The purpose of this paper is to present a revised hypothesis which, in essence, suggests that drinking and intoxication can be put in the service of psychic defense mechanisms against various sources of anxiety. Our case material, of which samples are presented, does not support a generalization that the immediate source of the anxiety is oral conflict. Instead, the anxiety being assuaged by the drinking appears to vary from one person to another. However, as the drinking episodes continue, the "pleasure" obtained from the intoxication can begin to supersede as goal the relief from the original anxiety. Ultimately, the psychodynamic conflict specific to the outset of the problem may come to be overshadowed by the "nonspecific" oral narcissistic elements.

My former colleagues in the Department of Psychiatry of the University of Cincinnati permitted the use of their case material.

EFFECT OF MEPHENESIN UPON ANXIETY

STANLEY L. BLOCK, M.D.
NORFOLK, VA.

MEPHENESIN (Myanesin, Tolserol),[1] one of a series of alpha-substituted glycerol ethers, was first investigated by Berger and Bradley [2] in 1946. Clinical interest in this compound arose after observations by the original authors [3] and by Stephen and Chandy [4] on its muscle-relaxant properties without significant alteration in consciousness. The drug is short-acting and rapidly inactivated. Its duration of action is variable. Gammon and Churchill [5] Stephen and Chandy,[4] and Spiegel and Wycis [6] stated the belief that the site of action is the subcortical nuclei. On the other hand, Henneman and Scherrer,[7] Kaada,[8] and Davison [9] reported the primary site to be the internuncial neurons of multisynaptic complexes. Reports have appeared on its clinical application in alcohol intoxication,[10] electroconvulsive therapy,[11] hyperkinetic and spastic disorders,[12] surgical anesthesia,[13] and tetanus.[14]

Surgeon (R), United States Public Health Service.

From the Medical Service, United States Public Health Service Hospital.

1. The drug used in this study was supplied by E. R. Squibb & Sons under the brand name of Tolserol.

2. Berger, F. M., and Bradley, W.: The Pharmacological Properties of α: β-Dihydroxy-γ-(2 Methylphenoxy)-Propane (Myanesin), Brit. J. Pharmacol. **1**:265-272 (Dec.) 1946.

3. Berger, F. M., and Bradley, W.: Muscle-Relaxing Action of Myanesin, Lancet **1**:97 (Jan. 18) 1947.

4. Stephen, C. R., and Chandy, J.: Clinical and Experimental Studies with Myanesin (Preliminary Report), Canad. M. A. J. **57**:463-468 (Nov.) 1947.

5. Gammon, G. D., and Churchill, J. A.: Effects of Myanesin upon the Central Nervous System, Am. J. M. Sc. **217**:143-148 (Feb.) 1949.

6. Spiegel, E. A., and Wycis, H. T.: Effect of 3-Ortho-Toloxy-1,2-Propanediol (Tolserol, Myanesin) upon the Electrogram of the Human Cortex and Subcortex, Proc. Soc. Exper. Biol. & Med. **72**:446-448 (Nov.) 1949.

7. Henneman, E., and Scherrer, J.: Mode of Action of Myanesin on Central Nervous System, Tr. Am. Neurol. A. **74**:208-211, 1949.

8. Kaada, B. R.: Site of Action of Myanesin (Mephenesin, Tolserol) in Central Nervous System, J. Neurophysiol. **13**:89-104 (Jan.) 1950.

9. Davison, M. H. A.: "Myanesin" as a Relaxant in Children, Brit. M. J. **1**:544-545 (March 20) 1948.

10. Herman, M., and Effron, A. S.: Tolserol in the Treatment of the Postalcoholic State, Quart. J. Stud. Alcohol **12**:261-267 (June) 1951.

11. Geer, F. D.: Effects of Oral Tolserol on Some Aspects of Electroshock Convulsions, Dis. Nerv. System **11**:27-29 (Jan.) 1950.

12. Berger, F. M., and Schwartz, R. P.: Oral "Myanesin" in the Treatment of Spastic and Hyperkinetic Disorders, J. A. M. A. **137**:772-774 (June 26) 1948.

(Footnotes continued on next page)

The purpose of the present study is to evaluate the effectiveness of mephenesin in ameliorating symptoms of anxiety. Reports have appeared concerning the use of this drug in a variety of psychiatric disorders, with special reference to its effect upon affect, restlessness, and anxiety. Schlesinger and associates,[15] and Stephen and Chandy [4] described mild euphoria and a "sense of well-being" following intravenous administration. Hay,[16] using a similar route, reported that it reduced agitation in a patient who had cerebral arteriosclerosis with psychotic manifestations and produced relaxation and mild euphoria in four schizophrenic patients and in two patients with manic-depressive psychosis, depressed type. Schlan and Unna [17] described improvement in anxiety symptoms in three patients taking mephenesin orally.

Dixon and associates [18] reported upon a series of 124 patients given mephenesin to relieve anxiety. The authors found that "in all except a very few, there was a dramatic and most satisfactory termination of the feeling of anxiety." On the basis of their data, they recommended that mephenesin be used to demonstrate relaxation to the patient as an adjunct to reeducative psychotherapy. Holt [19] reported that a patient with schizophrenia, paranoid type, showed notable improvement, with clearing of tension and reduction in agitation, while receiving mephenesin. Ten other psychotic patients showed no change. Holt concluded that mephenesin appeared to be of little value in controlling psychotic symptoms. Freudenberg [20] found it beneficial in anxiety states, but after two to three weeks the beneficial effects often subsided. Hecker and associates [21] reported the ability of mephenesin to release blocking in seven patients, to control rage in three patients, and to relieve tension in five patients tested.

PROCEDURE

Eleven patients were studied. The criterion for selection was the presence of anxiety as the chief symptom. No attempt will be made to define anxiety; rather, it is considered to be a group of objective signs and subjective symptoms which are generally accepted clinically. This

13. Mallinson, F. B.: New Synthetic Curarising Agent in Anesthesia, Lancet **1**:98-100 (Jan. 18) 1947.

14. Davison, M. H. A.; Ward, A. B., and Pask, E. A.: "Myanesin" in the Treatment of Tetanus, Brit. M. J. **1**:616 (April 9) 1949.

15. Schlesinger, E. B.; Drew, A. L., and Wood, B.: Clinical Studies in the Use of Myanesin, Am. J. Med. **4**:365-372 (March) 1948.

16. Hay, J.: Observations on the Use of Myanesin in Psychiatric Cases, Canad. M. A. J. **60**:224-226 (March) 1949.

17. Schlan, L. S., and Unna, K. R.: Some Effects of Myanesin in Psychiatric Patients, J. A. M. A. **140**:672-673 (June 25) 1949.

18. Dixon, H. H.; Dickel, H. A.; Coen, R. A., and Haugen, G. B.: Clinical Observations on Tolserol in Handling Anxiety Tension States, Am. J. M. Sc. **220**:23-29 (July) 1950.

19. Holt, W. E.: Effect of Mephenesin on Psychotic Patients, J. Nerv. & Ment. Dis. **115**: 343-350 (April) 1952.

20. Freudenberg, R. K.: Observations on Effect of Myanesin (3-Orthotoloxy-1,2 Propanediol or Tolserol) on Epileptic Thresholds and Some Psychiatric Conditions, J. Ment. Sc. **96**:751-757 (July) 1950.

21. Hecker, A. O.; Mercer, M., and Griffin, M. A., Jr.: Further Clinical Investigation of Tolserol (Myanesin), Dis. Nerv. System **12**:99-104 (April) 1951.

subject has been discussed by Cameron,[22] and his criteria were used in devising the check list of symptoms employed (tabulation). On admission to the hospital all patients were placed in an open psychiatric ward in order that the environmental factors might be controlled as much as possible. All received complete physical and psychiatric examinations, and routine laboratory work, including an x-ray study of the chest, serologic tests, urinalysis, and hemogram determi-

TABLE I.—*Summary of Results of Mephenesin*

Case No.	Sex	Age	Diagnosis	Dose, Gm. Q.I.D.	Effects	
					Mephenesin	Placebo
1	M	38	Anxiety reaction, severe	1.0	No objective change; subjective improvement	Objective and subjective improvement noted
2	F	26	Diabetes mellitus with tension headache and anxiety	1.0	Requested discontinuance after 1 wk.; no improvement	No objective or subjective change noted
3	M	18	Anxiety reaction, acute	1.5	No objective or subjective change noted	No objective or subjective change noted
4	M	19	Anxiety reaction, chronic	1.5	No objective or subjective change noted	No objective or subjective change noted
5	M	25	Anxiety reaction, chronic	1.5	No objective or subjective change noted	No objective or subjective change noted
6	F	32	Hysterical character disorder with conversion and anxiety	1.0	Slight objective improvement; subjectively worse	No objective or subjective change noted
7	M	19	Acute panic reaction	1.0	Slight objective improvement; subjectively worse	No objective or subjective change noted
8	M	24	Post-traumatic encephalopathy with anxiety	1.0	No objective change noted; subjectively worse	Slight objective and subjective change noted
9	M	30	Unorganized personality with anxiety	1.5	No objective change noted; subjectively worse	No objective or subjective change noted
10	F	26	Mixed psychoneurosis with phobias and anxiety	1.0	Discontinued after 1 wk. because of diarrhea and vomiting	.....
11	M	19	Anxiety reaction, chronic	1.0	Discontinued after 1 wk. because of diarrhea and vomiting	.....

* Results are listed according to the text, and not in the order tested.

nation. In addition, most of the patients had a Rorschach examination and later participated in clarification psychotherapy, so that the clinical and dynamic diagnoses were based on considerable information for each patient.

Objective Signs	Subjective Symptoms	
Biceps tendon reflex	Borborygmus	Diarrhea
Quadriceps tendon reflex	Internal tremors	Anorexia
Ankle clonus	Weakness and fatigue	Epigastric or abdominal sensations
Hoffmann sign	Generalized or nuchal stiffness	Bad oral taste or dry mouth
Tremor of outstretched hand	Head sensations	Feelings of anxiety or unreality
Tremor of closed eyelid	Jerking of limbs in sleep	Disturbances of thinking
Increased pulse rate	Tightening of throat	Jittery feelings or irritability
Blood pressure	Clicking in ears	Smothering sensations
	Blurred vision	Fears and phobias
	Precordial sensations	
	Nausea and vomiting	

The drug was supplied in 0.5 gm. tablets in coded bottles. Lot No. 1 was mephenesin; Lot No. *2* was placebo. The coding key was held by a disinterested party and was not consulted until the data were finally analyzed. The patient, the nursing staff, and I did not know whether mephenesin or placebo was being administered. All examinations were performed by me. Each patient served as his own control. Four weeks were used for the test: two weeks without medication; one week of Lot 1 medication, and one week of Lot *2* medication. The dosage used was 1.0 gm. four times a day for the first seven patients of the group and 1.5 gm. four times a day for the remainder. Observations were made and noted on the check list one to three times during each phase of the test period.

22. Cameron, D. E.: Observations on Patterns of Anxiety, Am. J. Psychiat. **101**:36-41 (July) 1944.

RESULTS OF TREATMENT

The results are summarized in Table 1. Only one patient (Case 1) reported subjective improvement. This improvement was noted during the mephenesin and placebo phase of the test and cannot be attributed to the direct action of the drug. In four patients (Cases 2, 3, 4, and 5) no objective or subjective change was

TABLE 2.—*Effect of Mephenesin on Individual Signs and Symptoms*

	Mephenesin			Placebo		
Signs and Symptoms	Improved	Unimproved	Worse	Improved	Unimproved	Worse
Biceps reflex						
Right	3	6	2	3	6	0
Left	2	7	2	3	6	0
Knee jerk						
Right	2	9	0	1	8	0
Left	1	10	0	1	8	0
Ankle clonus						
Right	1	10	0	1	8	0
Left	1	10	0	1	8	0
Hoffmann sign						
Right	1	10	0	1	8	0
Left	0	11	0	2	7	0
Tremor of hands	4	4	3	3	3	3
Tremor of eyelid	4	7	0	5	4	0
Pulse rate	1	8	2	2	6	1
Blood pressure	2	9	0	2	6	1
Borborygmus	3	6	2	1	4	4
Internal tremors	3	7	1	2	5	2
Fatigue	2	9	0	4	4	1
Weakness	2	9	0	4	5	0
Neck stiffness	1	9	1	1	8	0
General stiffness	1	9	1	1	8	0
Head sensations	0	10	1	2	6	1
Jerking limbs—sleep	1	9	1	1	7	1
Tight throat	1	9	1	1	7	1
Ear noise	0	9	2	0	8	1
Blurred vision	2	9	0	2	6	1
Chest sensations	1	9	1	2	7	0
Nausea	3	6	2	2	7	0
Vomiting	2	6	3	1	8	0
Diarrhea	0	9	2	1	6	2
Anorexia	1	8	2	2	6	1
Abdominal sensations	2	8	1	1	8	0
Bad oral taste	1	8	2	2	6	1
Dry mouth	0	9	2	1	8	0
Anxious feelings	2	8	1	3	5	1
Unreality feelings	2	6	3	1	7	1
Irritability	1	9	1	1	6	2
Thought disturbance	1	9	1	2	7	0
Fears and phobias	1	10	0	2	7	0
Jittery feelings	3	8	0	3	6	0
Smothering sensations	2	9	0	2	7	0

noted. Four patients (Cases 6, 7, 8, and 9) stated that they felt worse during the trial period with mephenesin, although no objective changes were noted. Since this change in subjective symptoms occurred with the drug and did not occur with the placebo, it may be presumed that the drug had some etiologic significance in making these patients feel worse. In two patients (Cases 10 and 11) the test was discontinued because of severe diarrhea and vomiting. Both these patients were receiving mephenesin at the time of appearance of these symptoms.

The data were further analyzed with respect to the effect of mephenesin on the individual signs and symptoms. These findings are summarized in Table 2. From these data it may be concluded that there is no significant change for any individual sign or symptom which could be attributed to the direct action of mephenesin.

COMMENT

Considering anxiety from the point of view defined in this paper, it may be concluded that if mephenesin is used alone (orally) in tablet form in the dosage of 1.0 to 1.5 gm. four times a day, little or no long-term ameliorative effect is to be noted. These findings would parallel the observations of Holt [19] in a group of psychotic patients; Dixon and associates,[18] who emphasized that mephenesin could not properly be used to relieve symptoms associated with an anxiety state, and Hecker,[21] who was of the opinion that the drug was not a therapeutic agent per se but could be used as an adjunct to more specific threapy. Reports are beginning to appear [23] that relaxation is induced by mephenesin for short periods and that it is useful in the release of blocking during a therapeutic session. Such a therapeutic possibility was not investigated in the present study.

It will be noted that two of the patients under observation were forced to stop taking the drug because of severe gastrointestinal disturbance. Attempts were made to prevent an irritant effect by always administering the drug with a full glass of milk. This prevention was not sufficient in the two cases cited. Bickers and associates,[24] Frantz,[25] Hay,[16] and Laurence [26] reported simliar experiences.

SUMMARY AND CONCLUSION

Eleven patients whose predominant symptom was anxiety were tested with mephenesin and placebo.

No significant amelioration of objective signs or subjective symptoms occurred.

It may be concluded that if mephenesin is used alone (orally) in tablet form in the dosage of 1.0 to 1.5 gm. four times a day, little or no long-term ameliorative effect is to be noted.

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23. Dixon and associates.[18] Hecker, Mercer, and Griffin.[21]

24. Bickers, D. S.; Cohn, G. A., and Rheinberger, M. B.: Progress in the Clinical Use of 3-(Ortho-Toloxy)-1,2-Propanediol (Mephenesin in Neurologic Disorders), New England J. Med. **242**:502-507 (March 30) 1950.

25. Frantz, C. H.: Orally Given Mephenesin in Infantile Cerebral Palsy, J. A. M. A. **143**: 424-426 (June 3) 1950.

26. Laurence, D. R.: Effect of Mephenesin in Spastic Paralysis, Lancet **1**:178-180 (Jan. 26) 1952.

XANTHOCHROMIA OF THE CEREBROSPINAL FLUID

II. Preliminary Description of Several New Colored Substances

R. M. N. CROSBY, M.D.
BALTIMORE
AND
GLENN L. WEILAND, Ph.D.
GETTYSBURG, PA.

XANTHOCHROMIA of the cerebrospinal fluid occupied a prominent place in the neurologic literature from the first description of its occurrence by Froin,[1] in 1903, until Scully's[2] review, in 1923. The importance of its occurrence as a diagnostic aid in disease of the central nervous system was stressed, and compilations of the specific diseases in which it appeared were made. Recently, fewer articles on this subject have been published because the mass of information accumulated by the earlier investigators was accepted and seemed to explain satisfactorily all instances of coloration of the cerebrospinal fluid. However, from recent clinical experience, it seemed unlikely in some cases that xanthochromia was produced by recognized pigment substances. A study of the pigments appearing in cerebrospinal fluid was therefore undertaken.

For the simplification of this study the xanthochromia of the cerebrospinal fluid produced in bacterial infection of the leptomeninges, carotenemia, and compression of the spinal cord was not considered. Other than the pigments produced in these conditions, textbooks of biochemistry,[3] pathology,[4] and clinical pathology,[5]

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Formerly Hoffberger Fellow and Hitchcock Fellow in Neurological Surgery (Dr. Crosby).

From the Departments of Neurological Surgery and Biological Chemistry of the University of Maryland School of Medicine and College of Physicians and Surgeons.

1. Froin, G.: Inflammations méningés avec réactions chromatique, fibrineuse et cytologique du liquide céphalo-rachidien, Gaz. d'hôp. **76**:1005, 1903.

2. Scully, F. J.: Yellow Spinal Fluid: Its Origin and Significance, Arch. Neurol. & Psychiat. **10**:83, 1923.

3. Cantarow, A., and Trumper, M.: Clinical Biochemistry, Ed. 3, Philadelphia, W. B. Saunders Company, 1945, p. 512. Everett, M. R.: Medical Biochemistry, Ed. 2, New York, Paul B. Hoeber, Inc., 1946, p. 559.

4. Minckler, J., in Pathology, edited by W. A. D. Anderson, St. Louis, C. V. Mosby Company, 1948, p. 1367.

5. Nicholson, D.: Laboratory Medicine: A Guide for Students and Practitioners, Ed. 2, Philadelphia, Lea & Febiger, 1934, p. 367. Osgood, E. E.: A Textbook of Laboratory Diagnosis, with Clinical Applications for Practitioners and Students, Ed. 2, Philadelphia, The Blakiston Company, 1935, p. 101. Kolmer, J. A., and Boerner, F.: Approved Laboratory Technique, Ed. 3, New York, Appleton-Century-Crofts Company, Inc., 1941, p. 300. Levinson, S. A., and MacFate, R. P.: Clinical Laboratory Diagnosis, Ed. 3, Philadelphia, Lea & Febiger, 1946, p. 575.

as well as articles in the recent literature,[6] agree that the only known coloring agents of the cerebrospinal fluid are hemoglobin and bilirubin. With gross bleeding into the cerebrospinal fluid the presence of hemoglobin is obvious, and its conversion to bilirubin has been experimentally demonstrated by Leschke.[7] The occurrence of these two compounds in other instances of xanthochromia is not as obvious, but few investigators have commented on the possibility of other colored substances being present. Jaguttis [8] studied the cerebrospinal fluid in cases of jaundice due to various causes and noted that the color disappeared from many of the samples on standing. Although no comment was made on the pigmented fluids in which the color persisted, those which faded were said to give a negative van den Bergh reaction. Samples of yellow cerebrospinal fluid were obtained from 60 newborn infants by Levinson, Greengard, and Lifvendahl.[9] Three of these gave a slightly positive benzidine reaction and only two had a positive van den Bergh reaction (indirect). Glaser [10] found that about 50% of samples of xanthochromic cerebrospinal fluid from 170 premature infants gave negative benzidine and van den Bergh reactions. To explain this finding, he postulated an intermediary between hemoglobin and bilirubin. Merritt and Fremont-Smith [11] suggested that a high protein content may cause coloration of the cerebrospinal fluid but did not present any data in confirmation and did not explain why only some samples with increased protein content are colored. Although these few investigators have questioned the occurrence of unknown coloring substances in xanthochromia of the cerebrospinal fluid, none has attempted to identify these substances which did not conform to the characteristics of either hemoglobin or bilirubin.

It is the purpose of this presentation to outline the preliminary study of several colored substances occurring in the cerebrospinal fluid which do not have the characteristics of a hemoglobin derivative or other porphyrin-containing compound.

MATERIAL

The samples of xanthochromic cerebrospinal fluid were obtained from the neurosurgical, medical, and pediatric services of the University Hospital and the Baltimore City Hospital and represented many varieties of disease of the central nervous system. All samples were checked for the presence of color, using a photoelectric colorimeter.[12] The benzidine reaction was desensitized so that a positive reaction was obtained only if hemoglobin was present in sufficient quantities to produce color, and all cerebrospinal fluid samples were checked by this method.[13]

6. Lange, C.: Methods for Examination of Spinal Fluid, Am. J. Syph. **23**:638, 1939. Merritt, H. H., and Brenner, C.: Clinical Examination of the Cerebro-Spinal Fluid: Outline, Wisconsin M. J. **45**:303, 1946.

7. Leschke, E.: Über die Gelbfarbung (Xanthochromie) der Zerebrospinalflüssigkeit, Deutsche med. Wchnschr. **47**:376, 1921.

8. Jaguttis, P.: Der Liquor bei Ikterus, Klin. Wchnschr. **6**:2143, 1927.

9. Levinson, A.; Greengard, J., and Lifvendahl, R.: Cerebrospinal Fluid in the New-Born, Am. J. Dis. Child. **32**:208, 1926.

10. Glaser, J.: Cerebrospinal Fluid of Premature Infants, with Special Reference to Intracranial Hemorrhage and Pigmentation, Am. J. Dis. Child. **36**:195, 1928; Cerebrospinal Fluid of Premature Infants: Results of a Series of Spinal Punctures in 170 Cases, with Special Reference to the Origin of Physiologic Xanthochromia of the New-Born Infant, ibid. **40**:741, 1930.

11. Merritt, H. H., and Fremont-Smith, F.: The Cerebrospinal Fluid, Philadelphia, W. B. Saunders Company, 1937, p. 56 and p. 160.

12. Crosby, R. M. N.; Alvarez de Choudens, J. A.; Thompson, R. K., and Weiland, G. L.: Xanthochromia of the Cerebrospinal Fluid: I. An Accurate Method of Quantitative Determination, Bull. School Med. Univ. Maryland **35**:62, 1950.

13. Robinson, F. H., and Miller, B. N.: On the Differentiation of Colored Cerebrospinal Fluids, Am. J. M. Sc. **191**:538, 1936. Crosby, R. M. N., and Smith, G. W.: Unpublished data.

Many samples were subjected to the van den Bergh test, but this procedure was later found to be superfluous because of the rarity of the occurrence of bilirubin without hemoglobin and so it was discarded in favor of solubility and absorption spectrum studies. All samples of cerebrospinal fluid colored by hemoglobin or bilirubin were eliminated from the study.

All samples were kept in individual containers at 5 to 10 C., and at no time were samples from different patients mixed. In order that the possibility of bacterial alteration of the pigment content might be eliminated, at least preliminary study of each sample of cerebrospinal fluid was made within 48 hours.

PROCEDURE; METHODS; RESULTS

Extractions.—An attempt was made to extract the coloring material from the samples of cerebrospinal fluid using solvents which were immiscible with water. Petroleum ether, diethyl ether, chloroform, benzene, ethyl acetate and *n*-butanol did not extract the color. Ethanol, methanol, acetone, and solutions of salts of heavy metals caused the precipitation of the protein contained in the fluid, and the colored material was precipitated with the protein or adsorbed on it. The color could not be removed from the precipitate by any method. This suggested the combination of the chromophore group with the protein; hydrolysis was therefore attempted, but the color was destroyed in the process.

Because of the possible porphyrin nature of the colored substance, extraction was tried with a mixture of glacial acetic acid and diethyl ether. Using a much higher proportion of acid than is necessary to extract porphyrins, the colored material appeared in the ether layer. To the sample of cerebrospinal fluid a few cubic centimeters of glacial acetic acid were added, and the mixture was then transferred to a separatory funnel containing diethyl ether. After the mixture was shaken, a thick gel formed. Glacial acetic acid was added, with shaking, until the gel disappeared and a distinct ether layer was formed. The relative quantities of acid and ether changed with different samples of cerebrospinal fluid because of the varying color and protein content, as well as the loss of ether by aqueous solution in the larger samples.

Acids of greater ionization than glacial acetic acid were tried in the acid-ether extractions to reduce the quantity of reagent needed. Both concentrated sulfuric and nitric acids destroyed the color in the few cerebrospinal fluid samples tested. Concentrated hydrochloric acid (C. P. reagent) was found not to affect the color and to make extraction with ether possible. With small amounts of this acid (less than 5% of the total volume of cerebrospinal fluid and ether) such a thick gel was formed that centrifugation was necessary to separate the ether layer. The use of larger quantities of hydrochloric acid resulted in an equilibrium which required many repeated single extractions or continuous liquid-liquid extraction. The exposure of the fluid extraction to daylight over long periods resulted in some loss of color from the sample, and in samples with very high protein content the formation of gel often stopped the extractor, so that a single repetitive extraction with glacial acetic acid was selected for routine, despite the large quantities of acid needed (often as much as 30% of the total volume of sample and ether).

Purification of Extracts.—Removal of the acid from the acid-ether extract was attempted first by neutralization. No matter what reagent was used, the neutralization of the acid resulted in marked decrease to complete loss of color. The use of an acid-binding resin (Amberlite IR-4B) was also unsatisfactory. Possibly because of the presence of a high concentration of ether, the acid-ether extract came through the resin column unchanged.

Chromatographic adsorption was tried, a white adsorbent being used in order that the presence of color could be noted. Of alumina (aluminum oxide cream), talc, and fullers' earth (an impure aluminum silicate) activated alumina was the only substance on which the color was adsorbed. Put on such a column in acetic acid-ether solution, the material showed three distinct bands: lemon-yellow, green, and dark-greenish-brown. Although many solvents and solvent pairs were used, the chromatogram could not be developed sufficiently to give adequate separation of the bands. Elution of the colored substances could be accomplished only with acidified ether. The bright-yellow material seen on the chromatogram became colorless in less than 30 minutes if exposed to light and in several hours if kept in the dark.

Distillation, followed by steam distillation of the acid-ether extract, was more successful. With the removal of the ether by distillation, some of the colored material appeared on the surface as an oily, lipid-like solid. More fatty solid material was precipitated when the pH of the extract was brought to between 4.0 and 4.5 by steam distillation. Although the remaining aqueous solution remained yellow, no more solid material could be recovered by further raising the pH. The solid material thus separated was readily soluble in diethyl ether. Small amounts of ether-soluble colored material could be recovered by shaking the yellow aqueous solution with ether, but much of the color remained in the aqueous fraction. Thus, two fractions, one ether-soluble and one water-soluble, were separated from the original acid-ether extract. On drying, both these fractions contained yellow-brown, lipid-like material.

Identifying Tests.—Both the aqueous fraction and the ether fraction had continuous absorption spectra in the visible wave length. The latter was also studied in benzene and chloroform without any absorption peaks being found. The absence of specific maxima most likely indicates the presence of several compounds in each fraction.

Neither fraction contained iron. On using *p*-dimethylaminobenzaldehyde after sodium fusion, each fraction gave a negative reaction for the pyrrole nucleus, so that any possible origin in hemoglobin or other porphyrin compound was eliminated.[14] To date, no reactive groups have been identified in either fraction.

The ether-soluble fraction gave a positive color reaction with *o*-dianisidine, indicating an aldehyde group,[15] but aldehyde derivatives could not be prepared with bisulfite, hydrazine, phenylhydrazine, or 2,4-dinitrophenylhydrazine. It is felt that color formation with the Schiff reagent was due to the presence of an unsaturated compound.[16]

Other Types of Coloring Material.—The cerebrospinal fluid samples containing substances extractable with the acid-ether mixture represent about 80% of the xanthochromic fluids examined. At least two other types of coloring material were found in the remaining samples. One of these was destroyed by the addition of all concentrated acids. The other colored substance was inextractable in the acid-ether mixture and was soluble only in water. Neither of the latter two types contained iron or bilirubin.

14. Feigl, F.: Qualitative Analysis by Spot Tests; Inorganic and Organic Applications, Ed. 3, New York, Elsevier Pub. Co., 1946, p. 340.

15. Feigl,[14] p. 383.

16. Chu, C. H. U.: A Histochemical Study of Staining the Axis Cylinder with Fuchsin-Sulfurous Acid (Schiff's Reagent), Anat. Rec. **108**:723, 1950.

CLINICAL EXPERIENCE

In the past three years over 200 samples of colored cerebrospinal fluid have been studied. Fluid samples from obvious cases of subarachnoid hemorrhage were not included. If the reactions to the benzidine and van den Bergh tests were negative, the sample was examined by extraction with glacial acetic acid and diethyl ether and classified in one of three groups of coloring materials described above. As an additional check, heating the acid-ether extract caused bilirubin to be oxidized to biliverdin, and the conversion of a yellow extract to a green one was accepted as indicating the presence of biliary pigment. The clinical occurrence of the three types of coloring material is listed in the following tabulation.

Extractable	Destroyed
1. Internal or communicating hydrocephalus	1. Occasional degenerative diseases of the spinal cord when active
2. Some intracranial neoplasms	2. Spinal subarachnoid block
3. Some cerebral degenerative diseases when active	Unextractable
4. Encephalomalacia associated with increased intracranial pressure	1. Some cases of serous meningitis (pseudotumor)
5. Loculated fluid in cerebral subarachnoid space	2. Some cases of distention of the subarachnoid space in infants

Frequently only the first sample of cerebrospinal fluid was found to be pigmented, and when the intracranial pressure was relieved the coloring material was no longer present.

Fluid from 10 cerebral gliomas has also been found to contain these hitherto undescribed coloring materials. The absence of colored hemoglobin derivatives in fluid from cystic gliomas has been confirmed by Cumings.[17]

CONCLUSIONS

It is believed that these non-porphyrin-containing colored substances occur in the cerebrospinal fluid as a result of the destruction of central nervous system tissue. This would explain their fat-like nature, as well as their transitory appearance during periods of active disease or increased intracranial pressure. It appears also, from results obtained so far, that the coloring substances deposited in the cerebrospinal fluid in destruction of cerebral tissue differ from those deposited in destruction of the spinal cord. It is hoped that further study of these compounds will yield a better understanding of the effect of certain disease processes upon the nervous system.

SUMMARY

In addition to hemoglobin, bilirubin, carotene, and pigments resulting from bacterial metabolism, one must add to the list of substances causing xanthochromia of the cerebrospinal fluid several lipid-like substances which apparently result from destruction of cerebral and spinal cord tissue. These fat-like substances are soluble in lipid solvents, contain neither iron nor pyrrole groups, and probably have several double bonds. They have a continuous absorption spectrum in the visible wave lengths.

17. Cumings, J. N.: The Chemistry of Cerebral Cysts, Brain **73**:244, 1950.

11 East Chase St. (2) (Dr. Crosby).

Gettysburg College (Dr. Weiland).

THIAMYLAL IN ELECTROCONVULSIVE THERAPY AND SIGNIFICANCE IN ANALYSIS OF SEIZURE MECHANISMS

RALPH S. GREEN, M.D.
AND
RUDOLF LEISER, M.D.
ELOISE, MICH.

SINCE the introduction of the convulsive therapies by von Meduna in 1935, many endeavors have been made to modify the resulting seizures in order to reduce complications and side-effects inherent in these forms of treatment. One of the methods used has been the administration of drugs designed to alter the convulsions in order to temper the undesired effects.[1] Drug modifications of electroshock therapy have been directed primarily in two channels. The first of these is the regulation of the muscle end-plate physiology in such a way as completely or partially to interrupt the nerve-muscle, conduction-response mechanism. The other approach is the alteration of cerebral physiology designed to (1) modify the course of the convulsion and (2) change the patient's reaction to the treatment. The present report deals with the latter.

It has been recognized for some time that any subcomatose or comatose state increases the convulsive threshold remarkably.[2] The drugs probably most widely used to induce such a state have been the various derivatives of barbituric acid. Since the barbiturates have a general type of depressant action on the cerebrospinal axis,[3] they were felt to be suitable in minimizing the three chief problems confronting the psychiatrist who administers convulsive therapies, namely, (1) management of the resistive and apprehensive patient who refuses treatment; (2) prevention of surgical and medical complications, and (3) management of postconvulsive excitement. Impastato and associates [4] administered amobarbital (Amytal) sodium intravenously prior to electroshock and reported favorably on the attenuated seizure. The intravenous use of thiopental (Pentothal) sodium, the so-called sleep-electroshock therapy, was described by Rubinstein.[5] He pointed out that the value of the drug

From the Psychiatric Department of the Wayne County General Hospital; Director Rudolf Leiser, M.D.

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2. Kalinowsky, L. B., and Hoch, P. H.: Shock Treatment, Psychosurgery and Other Somatic Treatments in Psychiatry, Ed. 2, New York, Grune & Stratton, Inc., 1952.

3. Goodman, L., and Gilman, A.: The Pharmacological Basis of Therapeutics, New York, The Macmillan Company, 1941.

4. Impastato, D. J.; Bak, R.; Frosch, J., and Wortis, S. B.: Modification of Electrofit: Sodium Amytal, Am. J. Psychiat. **100**:358, 1943.

5. Rubinstein, H. S.: Sleep-Electroshock Therapy of the Psychoses, Arch. Neurol. & Psychiat. **59**:517, 1948.

was in allaying apprehension and eliminating the postconvulsive excitement. Secobarbital (Seconal) sodium was felt to be indicated as premedication in electroconvulsive therapy by Gysin and Witham.[6] In 1950 Tarnower and Gladstone[7] studied the use of thiopental sodium for the prevention of musculoskeletal injuries in electroconvulsive therapy and found it effective.

The recent introduction of a new ultrashort-acting thiobarbiturate, thiamylal sodium (Surital[8]), led Brown[9] to study this drug as an adjuvant to electroshock treatment. He reported that this technique appeared to abolish or to minimize muscular activity, so that the treatment could safely be administered to patients who have bony lesions or cardiovascular complications that ordinarily contraindicate electroshock therapy. The reduction of the pretreatment apprehension was mentioned briefly.

Since in our experience the problem of pretreatment anxiety has at times made electroshock difficult, dangerous, or even impossible, our interest was aroused by this report. The advantages of the use of thiamylal over other barbiturates are primarily its rapid action and its short duration. For this reason, the anesthetic effect after recovery from the seizure was felt to be of minimal importance.

We had observed in previous clinical trials of barbiturates prior to electroshock that the postseizure apnea, i. e., the period between the cessation of the convulsion and the patient's first inspiratory effort, appeared to be prolonged. We were therefore apprehensive in using barbiturates in conjunction with electroshock. Pharmacologically, this effect should be expected, since in large doses barbiturates have a direct depressant action on the medullary respiratory center and, to a less degree, on the sinoaortic chemoreceptors.[3]

In the literature, however, few observations have been made regarding this prolongation of apnea. Impastato and associates[4] reported that "sodium amytal does not cause alarming apnea." Rubinstein[5] mentioned that "one must consider the danger of the simultaneous use of a barbiturate and electricity, either of which when administered in lethal quantities affects primarily the respiratory center in the medulla." No respiratory embarrassment following secobarbital sodium prior to electrotherapy was reported by Gysin and Witham.[6] Thiopental sodium as an adjuvant to this treatment was thought to shorten postconvulsive apnea and diminish cyanosis.[7]

Brown,[9] in working with thiamylal, observed that "the patients were less cyanotic immediately after shock" and commented, "The fact that the patients convulsed for a significantly shorter period with the thiamylal technique would also suggest that the brain is subjected to a shorter period of anoxia." The longer postseizure apnea was, however, not mentioned.

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6. Gysin, W. M., and Witham, R. G.: Use of Seconal Sodium in Electroconvulsive Therapy, Dis. Nervous System **10**:315, 1949.

7. Tarnower, S. M., and Gladstone, R. W.: Use of Pentothal Sodium in the Prevention of Musculoskeletal Injuries During Electroconvulsive Therapy, New England J. Med. **242**:653, 1950.

8. Trademark of Parke, Davis & Company for the sodium salt of 5-allyl-5-(1-methylbutyl)-2-thiobarbituric acid. The material for this study was furnished through the courtesy of Parke, Davis & Company.

9. Brown, E. O., Jr.: Use of Thiamylal (Surital) Sodium with Electroshock, A. M. A. Arch. Neurol. & Psychiat. **68**:43, 1952.

As these statements indicate, no specific or quantitative observations were made in regard to barbiturates in electroshock.

We first tried thiamylal in October, 1952. At that time it was used with an extremely apprehensive patient who refused shock therapy and fought actively and overtly against submitting to the treatment. He did not object, however, to the intravenous injection of the drug. We noted in this patient an alarmingly prolonged postseizure apnea and thereupon decided to study in detail the effect of thiamylal upon the course of electroconvulsive treatment.

PROCEDURE

Our series consisted of 20 male patients who were chosen at random from a group whose illness called for electroshock therapy. No special criteria for selection were used. An attempt was made to give each patient six treatments without thiamylal, to be followed by six treatments with the drug. In this way each patient served as his own control. A total of 121 ordinary electroshocks, or an average of 6 treatments per patient, and 111 electroshocks with thiamylal, or an average of 5.5 treatments per patient, were given.

In all cases a 2.5% solution of thiamylal sodium was injected intravenously at the rate of about 1 cc. per five seconds. By using this technique, we could be sure that the drug had reached its full effectiveness before more was administered. A sufficient amount was given to produce unconsciousness, as judged by absence of response to visual and auditory stimuli. We attempted not to abolish the corneal reflex. Doses required to reach this stage ranged from 0.2 to 0.375 gm. (8 to 15 cc.). The electric current was applied immediately upon the patient's reaching the required depth of anesthesia.

Data on the following factors were obtained in treatments both with and without thiamylal:

1. The setting of the electroshock apparatus, in milliamperage and time.

2. The "duration of the seizure," in seconds, as measured from the throwing of the "treat" switch to the cessation of any muscular contractions.

3. The duration of "postseizure apnea," in seconds, as measured from the last muscular contractions to the patient's first inspiratory effort.

4. The total period of apnea, in seconds, consisting of the sums of the duration of the seizure and the postseizure apnea.

5. The type of seizure (normal, subnormal, severe, Jacksonian, or abortive).

6. The "response time" measured to the nearest minute from the application of current to the regaining of consciousness, without regard for any confusion which may have been present at the time of response.

It was noted that the patients were anesthetized rapidly and smoothly. Only one exhibited excitement during the induction stage.

In the beginning of the study, our anxiety regarding the prolonged postseizure apnea led us to think of applying artificial respiration; but since we found that this period of apnea in no case exceeded 30 seconds, we purposely avoided any aid to respiration, such as artificial respiration or oxygen, except for the mechanical clearing of the air passage by pushing the mandible forward.

RESULTS

In treatments with thiamylal a significantly shorter duration of seizure was observed, while the duration of postseizure apnea was significantly increased. The total period of apnea in treatments with and without the drug, however, remained constant. The response time was markedly longer with thiamylal.

The accompanying Table presents our results. The data obtained from each patient were averaged, and the figures represented the means for all patients. The statistical method used in the analysis of the results was the calculation of the difference between correlated means, with correction for small samples, and involved the use of the t table.

While postconvulsive excitement was frequently seen in treatments without thiamylal, this stage was abolished in the same patients when electroshock was given in conjunction with the drug. The patients appeared somewhat less confused when awakening from the combined treatment than when awakening from the ordinary electroshock treatment.

Though they are, of course, difficult to quantitate, it appeared that psychiatric results with the use of electroconvulsive therapy were essentially unchanged by the addition of thiamylal. Of the 20 patients treated, 12 showed good, 7 fair, and 2 slight improvement.

All patients, while showing varying amounts of apprehension before ordinary electroshock therapy, exhibited less anxiety once the thiamylal treatments were started. They preferred, without exception, the "shot" to the "shock," though no particular attempt was made to hide the fact that the injecion would be followed by electroshock. This may, in part, be explained by the feeling of euphoria which the patients experienced upon the administration of thiamylal, a phenomenon already noted by Brown.[9] The one case in which thiamylal had to be given for extreme

Results of Treatment with Thiamylal

Factor	Treatments Without Thiamylal	Treatments With Thiamylal	Possibility of Chance Occurrence (Value of P)	Significance
Average duration of the seizure	37.7 sec.	23.5 sec.	<0.001	Significant
Average period of postseizure apnea	0.8 sec.	13.0 sec.	<0.001	Significant
Average period of total apnea	38.5 sec.	37.0 sec.	>0.1	Not significant
Average response time	5.9 min.	11.7 min.	<0.001	Significant

apprehension could not be included in this series, since it was impossible to treat the patient without preceding anesthesia, and he thus could not serve as his own control.

In most instances the time and/or milliamperage of the shock machine had to be increased to produce a seizure when thiamylal was used. None of the patients appeared to acquire a tolerance for the drug. Untoward reactions or complications were not encountered.

COMMENT

We observed that the convulsion after thiamylal and electroshock was different from that seen after ordinary electroshock. Usually, after the application of current a typical grand mal seizure occurs, consisting of a tonic contraction, followed by vigorous clonic movements, which abate gradually. The convulsion after thiamylal starts in similar fashion, with a tonic contraction, and is followed by clonic movements. Both these phases are decreased in intensity. Instead of a gradual decrease in the amplitude of the clonic contractions, however, the seizure stops suddenly, as if cut off sharply. Yet the apnea continues and, as proved by our data, persists for a time which makes the apnea in this treatment equal to the duration of the ordinary seizure plus the postseizure apnea. Thus, instead of a grand mal convulsion in miniature, thiamylal electroshock therapy causes a seizure different both in quantity and in quality. It may be likened to a pebble tossed into a pool of water, which causes concentric wave-like rings. If the medium which is disturbed is changed from water to, for example, oil, the waves are not only changed in height, but will also fail to

reach the point in the periphery of the pool which was reached by the water waves. This simile serves only in visualizing the differences in the seizures; it is not meant as an explanation of the phenomenon.

It may be postulated that the application of electric current across the brain causes respiratory arrest by "paralyzing" one or both of the following areas: the cortical respiratory center in Brodmann's Area 6a β which lies directly in the path of the electric current, and the respiratory center in the medulla. This effect is associated with the stimulation of the motor cortex, which results in the visible characteristic epileptiform muscular movements. Thiamylal and other barbiturates increase the convulsive threshold of the brain, as proved by many previous observations (for example, the use of phenobarbital in epilepsy), as well as our own data (the necessity to increase the output of the shock machine with thiamylal-electroshock therapy). The respiratory center(s), however, already nonfunctioning as the result of the application of electricity, is (are), as indicated by our study, not further affected by thiamylal (and probably other barbiturates). Thus, we may speak of a "constancy of total apnea." This constancy of total apnea is further evidenced by previous observations. Kalinowsky [2] stated: "When a long latent period with apnea precedes the convulsion, respiration sometimes returns before the clonic phase of the convulsion has ended." He also quoted Mueller [10] as observing that respiratory difficulties are more frequent after a subconvulsive response than after a generalized seizure. It is quite possible that these "complications" are actually apneas which are only apparently longer, since the dose of electricity, though not enough to produce the peripheral seizure, is sufficient to cause respiratory arrest.

Our own data indicate clearly (Table) that with the procedure outlined the total apnea is constant after electroshock regardless of whether or not thiamylal has been given prior to treatment.

The findings could be formulated as:

$$A = s + pa = s' + pa'$$

where A is the total period of apnea; s is the time of the seizure, pa is the time of the postseizure apnea, and s' and pa' are the modified values of s and p, referable to the same patient.

Thus, since the total time of apnea is a constant, a diminution of the seizure time would result in a corresponding extension of the postseizure apnea. This formula is, of course, based only on, and is directly applicable only to, our thiamylal data. If its application could be extended, however, it might be useful in explaining the period of apnea following abortive seizures, where s' is zero, or at least very small, and pa' therefore equals, or nearly equals, A. In cases in which the seizure is preceded by a period of apnea, pa' would then be a negative value, since the patient begins respiration before the seizure stops (Kalinowsky and Hoch [2]).

CONCLUSIONS

In order to explain our findings, particularly the constancy of the period of apnea in modified convulsions, we would propose the theory that electroconvulsive stimulation of the brain causes two independent, but partially coinciding, phases, namely,

10. Mueller, M.: Die Elektrokrampfbehandlung (Cerletti), 1941, cited by Kalinowsky and Hoch.[2]

(1) the stimulation of the motor cortex, which causes the commonly observed peripheral convulsion, and (2) the independent arrest of the respiratory center(s). The first phase is subject to modification by thiamylal, and possibly other barbiturates, while the second phase is not changed by this drug in doses causing unconsciousness but not sufficient to abolish the corneal reflex. The two phases must be mediated through different brain centers, and the latter (respiratory arrest) can be caused by lower doses of electricity than the former (peripheral convulsion). Thus is it possible to have a so-called abortive seizure in a patient with a total period of apnea equal to that of a full grand mal convulsion in the same patient.

If such a theory is to be accepted, experimental data must show that one of the above independent variables, i. e., (1) the electroshock effect on the motor cortex and (2) its effect on the respiratory center(s), can be changed without affecting the other. Our results indicate that the seizure time can be shortened without affecting the total period of apnea (Table); i. e., they are independent variables. The only possible logical explanation is that they are mediated through different mechanisms, and thus our data substantiate the theory which has been advanced.

The reason that these two phases have not been described previously lies probably in the fact that they overlap in most instances of convulsions. Through the use of thiamylal, which shortens the convulsive phase while leaving the phase of respiratory arrest unaffected, we have been able to differentiate the two.

Clinically, it may be concluded that the prolonged postseizure apnea seen with thiamylal and electroshock should not arouse fearful apprehension in the therapist, since we have shown that the total apnea to which the patient is subjected is not extended.

SUMMARY

1. A series of 20 patients receiving both electroshock and thiamylal (Surital) sodium preceding the electroconvulsive treatment is reported.

2. Thiamylal changes the seizure by shortening its duration and prolonging the postseizure apnea.

3. The total period of apnea tends to remain constant in treatment both with and without thiamylal.

4. Thiamylal given prior to electroshock helps in preventing pretreatment apprehension and postconvulsive excitement.

5. Psychiatric improvement of patients receiving thiamylal-electroshock therapy was essentially that expected after treatment with ordinary electroconvulsive therapy.

6. A theory is proposed stating that the peripheral convulsion in electroshock is independent of the respiratory arrest and that these two phases are mediated through different brain centers. Data are presented in support of this theory.

ELECTROENCEPHALOGRAPHIC FINDINGS ASSOCIATED WITH SUBDURAL HEMATOMA

Review of Forty-Five Cases

ERNST A. RODIN, M.D.

REGINALD G. BICKFORD, M.B.

AND

HENDRIK J. SVIEN, M.D.

ROCHESTER, MINN.

IN PAST years the literature on subdural hematoma has been steadily increasing. Since Walter's [1] original description of a "silent area" over an extradural hematoma as evidenced in the electroencephalogram, and the description, by Jasper and co-workers,[2] of a "silent area" on the side of a subdural hematoma, several series of cases of subdural hematoma have been reviewed by various authors. These reviews have resulted in varied pictures. This discrepancy may be due to two factors: One is a matter of terminology. Both Walter and Jasper and co-workers employed the term "silent area," but Walter described under this term a delta focus, whereas Jasper and co-workers employed it for a marked lowering of the amplitude. A second factor is the small number of cases in most of the series. Glaser and Sjaardema [3] reported 3 cases; Cohn and co-workers,[4] 6 cases; Marsh and co-workers,[5] 13 cases; Smith and co-workers,[6] 7 cases; Friedlander,[7] 17 cases, plus 22 additional cases from the literature, and Sullivan and co-workers,[8] 32 cases.

Fellow in Neurology, Mayo Foundation (Dr. Rodin).

From the Section of Physiology (Mr. Bickford) and the Section of Neurologic Surgery (Dr. Svien), Mayo Clinic.

1. Walter, W. G.: Traumatic Extradural Haemorrhage: II. Clinical Application of Electro-Encephalography, Bristol Med.-Chir. J. **57**:86-90 (Summer) 1940.

2. Jasper, H. H.; Kershman, J., and Elvidge, A.: Electroencephalographic Studies of Injury to the Head, Arch. Neurol. & Psychiat. **44**:328-350 (Aug.) 1940.

3. Glaser, M. A., and Sjaardema, H.: Electro-Encephalographic Diagnosis of Extradural and Subdural Hemorrhage, Proc. Soc. Exper. Biol. & Med. **47**:138-140 (May) 1941.

4. Cohn, R.; Raines, G. N.; Mulder, D. W., and Neumann, M. A.: Cerebral Vascular Lesions: Electroencephalographic and Neuropathologic Correlations, Arch. Neurol. & Psychiat. **60**:165-181 (Aug.) 1948.

5. Marsh, C.; Hjartarson, G. D., and Courville, C. B.: The Electroencephalographic Findings in Subdural Hemorrhage and Hematoma: Review of the Literature and Report of 13 Cases, Bull. Los Angeles Neurol. Soc. **14**:163-181 (Sept.) 1949.

6. Smith, G. W.; Mosberg, W. H.; Pfeil, E. T., and Oster, R. H.: The Electroencephalogram in Subdural Hematoma, with a Review of the Literature and the Presentation of 7 Cases, J. Neurosurg. **7**:207-218 (May) 1950.

7. Friedlander, W. J.: The Electroencephalographic Findings in 39 Surgically Proven Subdural Hematoma, Electroencephalog. & Clin. Neurophysiol. **3**:59-62 (Feb.) 1951.

8. Sullivan, J. F.; Abbott, J. A., and Schwab, R. S.: The Electroencephalogram in Cases of Subdural Hematoma and Hydroma, Electroencephalog. & Clin. Neurophysiol. **3**:131-139 (May) 1951.

In general, the investigators just mentioned drew attention to (1) suppression of the alpha rhythm on the side of the lesion, (2) focal slow-wave activity, and (3) occurrence of normal records. Friedlander [7] went further in pointing out that there are six types of records that may occur. In addition to the above-mentioned three types, he observed (1) diffuse, nonfocal slow waves, (2) focal abnormal slow waves whose amplitude is equal to or greater than the base-line voltage on the opposite side, and (3) focal low-voltage rhythm with high-voltage activity surrounding it. He found that focal slow-wave activity occurred in 56% of cases, and some type of focal abnormality that helped in the diagnosis raised the total to 67%. An abnormality, focal or not, was found in 92%, whereas normal records were encountered in 8%. He found a focal low-voltage electroencephalographic pattern to be associated with only those subdural hematomas that were located in the temporal or temporoparietal areas, but he added a word of caution, namely, that the surgeon is frequently unable to assess accurately from the burr holes the exact extent of the lesion. Friedlander concluded that "hypopotentia" (by which he apparently referred to unilateral reduction of amplitude) in a routine electroencephalogram is not a significant finding in cases of subdural hematoma.

Sullivan and co-workers,[8] in their series of 32 cases, found only evidence of suppression of alpha waves and the presence of focal slow-wave activity in their records. The electroencephalograms lateralized correctly in 75% of cases and localized correctly in 47%. Attention was drawn to the absence of paroxysmal discharges as a useful sign in diagnosis. Suppression of the alpha rhythm was called a specific finding. In their series, suppression of the alpha activity was found, however, to be associated not only with posteriorly located hematomas, but also with anterior ones in five cases. Disappearance of the electroencephalographic abnormality seemed to be correlated with the clinical postoperative recovery. When recovery was slow, the abnormalities persisted, and there were clinical residuals. When clinical recovery was complete, the electroencephalographic abnormalities had returned to normal.

In the group of Marsh and co-workers,[5] a diagnosis as to the side was made correctly in six of nine cases. The occurrence of false localizations was observed, and distortion and dislocation of the brain, counterpressure, and transmission of abnormal discharges through commissural and association bundles were held responsible for these errors.

Smith and co-workers [6] claimed that electroencephalographic abnormalities depend on the amount of bleeding, the location, and the time interval between bleeding and electroencephalographic recording. This postulation was made on the evidence provided by experimental subdural hematomas produced by Cohn [9] in cats and by Ulett [10] in dogs. Smith and co-workers [6] were able to make a correct diagnosis in all their seven cases on the basis of a pronounced lowering of the amplitude and low-voltage slow waves over the affected hemisphere. They blamed an "atypical" record on failure to employ bipolar recording technique. The authors stated, further, that "variations might also be explained by concomitant intracranial hemorrhage and/or brain damage."

9. Cohn, R.: Subdural Hematoma: An Experimental Study, Arch. Neurol. & Psychiat. **59**:360-367 (March) 1948.

10. Ulett, G.: Electroencephalogram of Dogs with Experimental Space-Occupying Intracranial Lesions, Arch. Neurol. & Psychiat. **54**:141-149 (Aug.) 1945.

The only article on subdural hematoma in infants and children which we could find in the literature was that by Marinacci and co-workers.[11] They reported on a group of seven infants, aged 2 to 18 months, and one child, aged 4 years. Four patients had focal hemispheric electroencephalographic abnormalities, and three had diffuse abnormalities. The authors concluded that the electroencephalographic findings are not pathognomonic for subdural hematomas in infants and children, but are of help in the diagnosis of cerebral lesions.

Our interest in this subject was aroused by the frequent complexity of the recordings in cases of subdural hematoma and the occurrence of bilaterally synchronous discharges in the presence of a unilateral lesion. This aspect of the subject seems to have received little attention in the literature.

MATERIAL AND METHODS

We reviewed all the cases of subdural hematoma at the Mayo Clinic in which an electroencephalogram had been recorded prior to operation in the period from Jan. 1, 1948, to Oct. 31, 1952, inclusive. From these cases we selected those in which the hematoma as seen at operation was not associated with cortical laceration. In 7 of the 45 cases so selected the patient had sustained a head injury or had the onset of symptoms 7 to 14 days before the electroencephalogram was recorded; in 5 cases the interval was 1 month, and in the remaining 33 cases the intervals varied from 2 months to 3 years. Most of these recordings were taken three to four months after the initial onset of the symptoms or head injury. In this series, therefore, we are dealing mostly with chronic subdural hematoma.

In the entire series of 45 patients, there were 39 males and 6 females. There were 5 infants, aged 2½ months to 1 year, and 3 children, 1 to 10 years of age; the rest were adolescents, 10 to 20 years of age, or adults, of ages ranging up to 75. Twenty-four patients were in the age group of 50 to 75. Twenty-eight had a history of trauma. In the nontraumatic group there were three alcoholics and one epileptic (seizure trauma?). Thirty-four patients had a unilateral hematoma. In the total group one patient had an extradural hematoma and nine a subdural hygroma; but since these patients did not show patterns that were different electroencephalographically or clinically from those of the other patients, they were not placed in a separate group.

All the recordings were taken on an eight-channel Grass ink writer. Five pairs of parasagittal scalp electrodes were spaced at equal intervals between the glabella and the inion. An additional Sylvian electrode on either side was placed vertically 2½ in. (6.3 cm.) above the external meatus. Both scalp-to-scalp and scalp-to-ear recordings were used routinely.

The effect of mental activity (simple calculations) on the recording was observed in 10 cases; the effect of three minutes of hyperventilation, in 22 cases, and the effect of photic stimulation, in 37 cases. The source of light was a Strobotron-type flash tube (intensity, 250,000 f.-c.). It was used at a distance of 6 in. (15 cm.) from the eyes. The rates were 1, 3, 6, 8, 9, 10, 11, 12, 15, 20, and 30 flashes per second. The patients were exposed to the light stimulus at each of these flicker rates for 10 seconds and were tested with eyes both open and closed.

In this study the term "delta waves" was applied to random irregular slow waves with a frequency of 0.5 to 3 cps, which were relatively unaffected by opening the eyes. The term "dysrhythmia" was applied to rhythmic medium-voltage to high-voltage slow waves of 3 to 5 cps which appeared in bilaterally synchronous paroxysms and tended to be inhibited by opening the eyes, as well as less rhythmic low-voltage to medium-voltage waves in the theta frequency range.

RESULTS

Since the interpretation of children's records presents considerable difficulty, we felt it wise to separate our cases into two groups: (1) those of infants and children up to the age of 10 years, and (2) those of adolescents and adults. The

11. Marinacci, A. A.; Rand, C. W., and Marinacci, H. K.: Electroencephalographic Findings in Chronic Subdural Hematoma of Infancy and Early Childhood, Bull. Los Angeles Neurol. Soc. **16**:255-266 (Sept.) 1951.

classified findings in Group 1 are given in Table 1. It is evident that the electroencephalogram was not very helpful in localizing the three unilateral hematomas but was more effective in indicating the presence of an organic lesion in the cases in which bilateral hematoma was present. It was especially disappointing to see the rarity with which a significant unilateral reduction of amplitude could be found. The number of cases involved is, however, too small to be statistically significant.

TABLE 1.—*Classified Electroencephalographic Findings in Eight Infants and Children Aged 2 Months to 10 Years*

	Electroencephalographic Findings				
Lesion	Normal	Focal Delta Waves	Bilateral Delta Waves	Asymmetry	Atypical Spike Waves
Unilateral subdural hematoma	1 (Slightly asymmetric; flatter on side of lesion)	1 (Symmetric background; delta on wrong side; possible artifact)	1 (Symmetric background)	.....	.....
Bilateral subdural hematoma	1 (Much movement artifact; symmetric background)	1 (Asymmetric background; flatter on side of larger lesion)	.....	1 (Suppression on side of larger lesion)	1 (Symmetric background)
.....	.....	1 (Symmetric background)	.....	.....	.....

TABLE 2.—*Classified Electroencephalographic Findings in Thirty-Seven Adolescents and Adults* *

		Total No.
Normal Records		2
Increased episodes of drowsiness	1	
Alpha asymmetry, but suppression on normal side	1	
Focal or bilateral delta waves with maximal incidence on one side		26
Delta focus on normal side	2	
Delta bilateral but maximal on normal side	1	
Delta focus on side of subdural hematoma	23	
Bilateral delta waves with no lateralization		5
No localizing features	2	
Delta slower on side of subdural hematoma	1	
Background flatter on side of subdural hematoma	2	
Dysrhythmia		4
No localizing features	4	

* Electroencephalogram localized hematoma in 70.2%, did not localize lesion in 29.8%.

The single finding of an atypical spike-wave pattern in a 3-year-old child cannot lead to any conclusions, since generalized seizures had developed five months before evacuation of bilateral subdural hygroma. No follow-up record was obtained, and it is therefore uncertain whether the case was one of subdural hygroma in a patient with idiopathic epilepsy or whether the hygromas had actually given rise to the spike-wave pattern, though the former suggestion seems more probable.

Table 2 gives the findings in Group 2, that of adolescents and adults. It can be seen that the electroencephalogram localized the lesion in 70.2% of the cases and did not aid in localization in 29.8%. These percentages refer to unilateral and bilateral

subdural hematoma. For bilateral hematoma, the maximum of abnormality was usually on the side of the larger clot; in one case, however, it was on the side of the smaller one.

Since bilateral subdural hematoma is more likely to give a greater electroencephalographic disturbance, the percentages of proper localizations, wrong localizations, and nonlocalizations were calculated separately for unilateral and bilateral subdural hematoma. The findings are given in Table 3. The factor which led to wrong localizations was a difference in amplitude, the higher amplitude being on the normal side. When the presence of a subdural hematoma is suspected, it can be argued that there is not an increase of discharges on the normal side but, rather, a suppression on the side of the lesion. When there is no history of trauma, however, and the presence of a brain tumor is suspected clinically, this spurious interpretation is easily made. It was found helpful in these instances not to rely on the difference of amplitude to determine which side was the affected, or most affected, one but to base the diagnosis on the frequencies involved. The side which showed the slower

TABLE 3.—*Electroencephalographic Findings in Thirty-Four Cases of Unilateral Subdural Hematoma*

EEG	No. of Cases	Percentage
Localized	19	55.9
Did not localize	10	29.4
Localized incorrectly	5	14.7

TABLE 4.—*Electroencephalographic Findings in Entire Group of Forty-Five Cases*

EEG	No. of Cases	Percentage
Localized	28	62.2
Did not localize	12	26.7
Localized incorrectly	5	11.1

delta waves was the side of the hematoma in the cases of a unilateral lesion or the side of the larger hematoma in the cases of bilateral lesions.

The findings as to the helpfulness of the electroencephalogram in the entire series are given in Table 4. The percentage of localizations is higher than that in the previous group, cases of unilateral subdural hematoma, because included are the bilateral subdural hematomas, lateralization of the larger ones of which is indicated by the electroencephalogram. The percentage, however, is lower than in the group of adolescents and adults (Table 2).

It was interesting to note that in only two of the five cases in which the electroencephalogram showed the maximal incidence of abnormality on the wrong side had head injuries been sustained. In these two cases one could postulate that the abnormality on the side opposite the hematoma might have been due to cortical damage as a contrecoup effect at the time of injury. This explanation is not valid in the three cases of spontaneous hematoma, and other factors may have been at work.

The clinical findings permitted correct lateralization in two of the five cases just mentioned. In one case lateralizing signs were not present. In the remaining two

cases there were bilateral pyramidal tract signs, which were stronger ipsilateral to the lesion. This finding gave the erroneous impression that there might be either a bilateral subdural hematoma or a unilateral hematoma on the side opposite that of the stronger pyramidal signs. In both cases the patient had a nontraumatic lesion—a unilateral hematoma on the same side as the maximal pyramidal signs. The significance of these findings will be discussed later.

Alpha or Background Asymmetry.—In the adolescent and adult group there were 32 cases in which the alpha rhythm was sufficiently well developed to permit judgment of the presence of derangements. The findings, correlated with the surgical

TABLE 5.—*Suppression of Alpha Waves Correlated with Various Regions of the Head in Thirty-Four Adolescents and Adults*

EEG	Region of Head							Total No. of Cases
	Entire Hemisphere	Fronto-tempo-parietal	Parieto-occipital	Temporo-occipital	Parietal	Frontal	No Data	
				Unilateral Subdural Hematoma				
Unilateral suppression	2	7 (suppression on side opposite lesion, 1)	2	..	2	..	..	13
Bilaterally symmetric alpha but poorly developed	3	2	..	1	..	1	..	7
No alpha change	..	3	..	..	..	1	..	4
Alpha slowed on side of lesion	1	..	..	..	..	1	..	2
Alpha absent	1	1	..	..	..	..	..	2
Subtotal	7	13	2	1	2	3	..	28
				Bilateral Subdural Hematoma				
No alpha change	1	..	..	..	1	..	..	2
Suppression on side of larger lesion	..	1	..	..	..	..	1	2
Suppression on side of smaller lesion	..	1	..	..	..	..	..	1
Unilateral suppression with equal amounts of fluid on two sides	..	..	..	..	..	..	1	1
Subtotal	1	2	..	..	1	..	2	6

location of the hematoma (Table 5), indicate that no clear-cut pattern emerged. In three instances there was no alpha rhythm, but a regular low-voltage to medium-voltage background activity of 6 to 7 cps was present. In one case this was symmetric; however, the surgeon did not indicate the exact site of the hematoma. The background activity was asymmetric in two cases; in one of these the hematoma was in the temporoparietal region, but in the other the location was, again, not specified. In two cases there was no alpha rhythm and no regular background activity. The percentage for suppression of alpha or background activity in the presence of unilateral hematoma was 48.3, and for asymmetrical records in cases of both unilateral and bilateral hematomas it was 48.1.

Photic Stimulation.—The responses to photic stimulation in 37 cases are summarized in Table 6. It shows that asymmetries of amplitude and persistence of the photic responses are not reliable indices to lateralization. There may be a bilaterally symmetric response to photic stimulation in the presence of a unilateral hematoma or a unilateral diminution of the photic responses in the presence of bilateral hema-

toma. It also shows that asymmetry of the alpha rhythm does not always correspond with asymmetry of the photic response. This can be taken to indicate some independence of the two systems. There seems, however, to be a more significant relation between the suppression of the photic response and the occurrence of a delta focus. Of the cases in which there was a better photic response on the side of the subdural hematoma, there was only one of focal delta activity, whereas in the group in which better responses were shown on the normal side there were six cases of focal delta waves. However, the groups are too small to allow any definite conclusions, and the masking effect which the delta waves might exert on the photic response has also to be considered. One patient, a child who had atypical spike-wave responses in the resting record, showed an augmentation of this pattern during photic stimulation.

Effect of Mental Activity and Hyperventilation.—In 10 cases the effect of mental activity on the recording was studied. In all 10 the resting record presented dysrhythmic components. Mental stimulation seemed to suppress the delta activity

TABLE 6.—*Electroencephalographic Responses to Photic Stimulation in Thirty-Seven Cases*

Photic Response	Cases	
	Total No.	Details of Response
None or poor (5 children less than 10 yr. old)	14	Alpha symmetry, 4; alpha asymmetry, 5; unilateral delta focus, 4; bilateral delta, 7
Equal on two sides	9	Alpha symmetry, 5; alpha asymmetry, 3; unilateral delta focus, 4; bilateral delta, 4
Better on normal side or on side of smaller hematoma	8	Alpha symmetry, 1; alpha asymmetry, 5 (alpha better on side of hematoma, 1); unilateral delta focus, 6; bilateral delta, 1 (bilateral hematoma, 1)
Better on side of hematoma	6	Alpha symmetry, 2; alpha asymmetry, 4 (alpha better on side of hematoma, 1); unilateral delta focus, 1; bilateral delta, 2

somewhat in one case and to reduce the amount of dysrhythmic activity in four cases, and it increased the alpha rhythm in one case. We interpreted these findings on an arousal basis (Fig. 1). In the one case in which the alpha rhythm was increased by mental activity episodes of drowsiness had occurred in an otherwise normal record. In four cases the mental activity did not cause any appreciable effect. In no instance did the abnormal activity become more pronounced.

Hyperventilation was carried out in 22 cases. A generalized increase in the abnormalities was noted in three cases, an increase in the dysrhythmic components in five, an increase in delta activity in seven, an increase in drowsiness in one, and no appreciable change in six.

Dysrhythmias and Mental Status.—Dysrhythmic components were present in the records of 24 of 37 adolescents and adults (Fig. 2). There was no correlation between the location of the hematoma or the duration of symptoms and the occurrence of dysrhythmia. There was also no correlation between dysrhythmic activity and the traumatic or nontraumatic nature of the lesions. There was, however, a correlation between the mental status of the patient and the dysrhythmia. In 26 of the 37 cases the patient showed some mental derangement, which was classified as mental slowing, drowsiness, disorientation, confusion, or coma. In 2 of the 26 cases dysrhythmic patterns did not appear in the records. In one of these the

mentioned episodes of drowsiness were manifested in the recording, and in the other a delta focus was exhibited on the side of the larger of bilateral subdural hematomas. In three cases in which the record showed dysrhythmia the patients were classified as mentally normal. Another feature we observed was the tendency of the abnormality to wax and wane. This was a prominent finding in seven cases, in two of which the patients were comatose, in three somnolent, and in two mentally slow. It was observable, though less pronounced, in 10 additional cases. In one case the patient was comatose; in one, semiconscious; in one, drowsy; in two, mentally slow; in four, confused, and in one, normal.

Postoperative Recordings.—Postoperative recordings were obtained in seven cases. In four cases these recordings were taken 7 to 11 days after evacuation of the hematomas. These records showed that there had been a decided tendency for the alpha rhythm to return, but it was still asymmetric, being less persistent and smaller in amplitude on the side of the previous hematoma. The delta foci were invariably present but evidenced less spread to other regions of the head. Theta

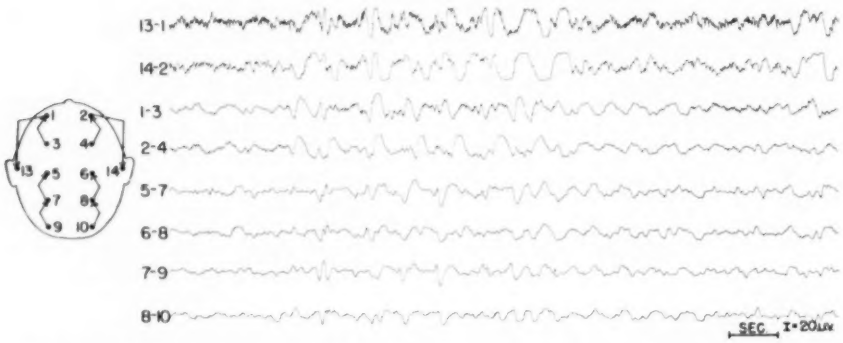


Fig. 1.—Electroencephalographic tracings from a man aged 52 who had sustained an injury of the head six months prior to admission. He had had headaches and somnolence for a few days. On examination the patient appeared somnolent, and the reflexes of the right arm were more active than those of the left. Multiple burr holes were made, and 250 cc. of blood from the convexity of the right hemisphere was evacuated. The patient made an uneventful recovery. The effect of talking to the patient on the dysrhythmic activity is to be noted.

frequencies were still present in three cases, in all of which slight mental derangement was still evident. In one case the electroencephalogram was taken three weeks after operation, before the patient was dismissed from the hospital, when the patient himself felt well but the neurosurgeon noted that some aphasia was still present. The alpha rhythm had returned in this instance to an apparently normal level, and the delta activity had become smaller in amplitude and was visible only on the side of the previous hematoma, whereas before it had been bilateral.

This finding seems to indicate that it takes about 14 days for the alpha rhythm to return to normal after removal of the clot, whereas it takes considerably longer for the delta focus to disappear. The persistence of delta waves for several weeks after operation is a reminder that the restitution of normal function is not completed with the removal of the hematoma. Clinical evidence, such as the presence of mild aphasia in one of the patients, supports this interpretation.

Two cases were of interest because sharp-wave foci developed after operation. The preoperative recording in the first case, one of chronic alcoholism, disclosed a correctly localized delta focus. A recording made 12 months after operation showed a sharp-wave discharge located below the old parietal burr hole on the side opposite

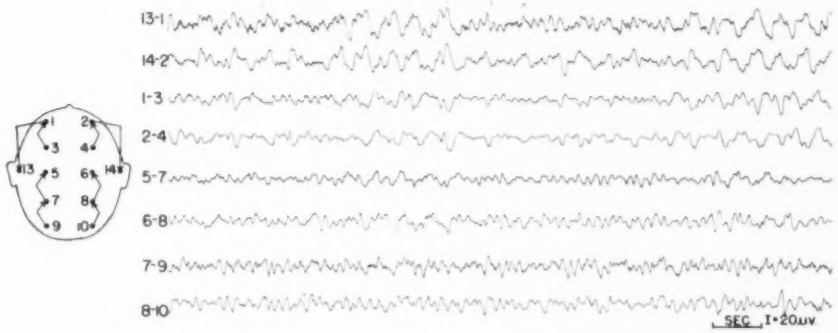


Fig. 2.—Electroencephalographic tracings from a man aged 54 who had sustained an injury to the head one year prior to admission. Four weeks prior to admission he had a grand mal convulsion. He had had headaches for a week. The patient appeared mentally slow on examination and had a memory defect. He was less dexterous with the left extremities than with the right. The pneumoencephalogram disclosed displacement of the brain to the left, and craniotomy revealed a large subdural hematoma on the right side, extending from the frontal to the occipital pole and down beneath the temporal lobe. The clot was evacuated and the patient made an uneventful recovery. The symmetry of the tracings in the presence of this unilateral lesion is to be noted.

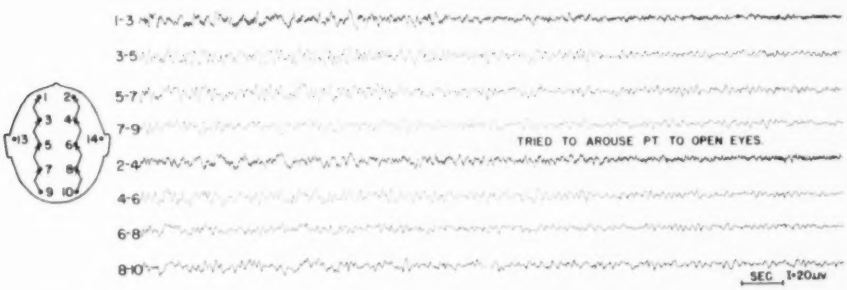


Fig. 3.—Electroencephalographic tracings from a woman aged 57 who had had grand mal seizures for 15 years. During the preceding four weeks she had had increasing mental apathy, sleepiness, and, finally, coma. The pneumoencephalogram suggested the presence of a lesion in the parasagittal plane of the right frontal lobe. Craniotomy disclosed that the entire right hemisphere was covered by a thick clot, which was evacuated. The patient remained comatose and died two days later. Necropsy revealed a residual of the right subdural membrane and also evidence of recent and old hemorrhage in the midbrain and pons. The symmetry of the recording and the appearance of dysrhythmic activity in paroxysmal bursts are to be noted.

the previous hematoma. This anomalous location could be explained on the basis of diffuse cortical atrophy (as indicated by pneumoencephalography). The possibility of an added factor of surgical trauma when the burr hole was drilled has also to be entertained. In the second case, in which the patient had suffered from automatisms since his head injury, a bilateral dysrhythmia Sylvian in distribution was present

before operation, and 27 months after operation a left Sylvian sharp-wave discharge was found to have developed. In this case there seems to be reasonable grounds for supposing that scarring following either the original head injury or the evacuation of the hematoma was responsible for appearance of the focal discharge.

These two cases illustrate the complexity of etiologic factors that may be involved in postoperative states and suggest the need for careful integration of clinical and electroencephalographic material.

In one case necropsy was performed two days after evacuation of a massive right-sided hematoma, which covered the entire hemisphere. A preoperative record showed almost complete absence of the alpha rhythm. Where it was present, it was symmetric. There were bitemporal medium-voltage slow waves and, in addition, paroxysmal bilaterally synchronous high-voltage waves of 2 to 4 cps, which appeared at times only in the motor and parietal areas but at other times were generalized in all regions of the head. These waves exhibited a pronounced tendency to wax and wane, the recording becoming nearly normal at times (Fig. 3). Localization or lateralization was not possible from this recording. Necropsy revealed the residual of a right-sided subdural membrane, pronounced compression of the brain on the right, and two points of recent and old hemorrhage in the pons and midbrain. In this instance the dysrhythmia of the projected type was apparently due to the hemorrhagic disturbance in the midbrain and pontine structures.

COMMENT

Alpha Asymmetry and Focal Slow Waves.—The findings with respect to alpha asymmetry and local slow waves in this series agree with those in the larger series in the literature. It was apparent that the location of the focal slow waves is more important than differences in amplitude in localizing the lesions, since the latter were not invariably present and might, as has been pointed out, be even misleading at times. It was also found important to judge the alpha symmetry on the basis not only of the amplitude but also of persistence and frequency, since the less persistent, and at times slower, alpha rhythms were usually found on the side of the lesion.

Smith and co-workers [6] called the suppression of the alpha rhythm on the side of the hematoma a specific finding in cases of subdural hematoma. However, Levy and co-workers,[12] who tried to make a diagnosis of subdural hematoma on the basis of the initial record, without using clinical data, found that a differentiation of "simple" closed head injury and subdural hematoma was impossible. In both instances suppression of alpha activity and focal slow waves were found. The authors also made the observation that the reduction of alpha rhythm persisted for a time after removal of the hematoma. Our patients showed an asymmetry of alpha rhythm up to 11 days after operation. These observations are difficult to reconcile with the "short-circuit" theory, which implicates the layer of fluid between the brain and the recording electrodes in the production of asymmetry of the record. It seems to make more likely the presence of an additional metabolic disturbance within the brain itself which causes the suppression of alpha activity.

12. Levy, L. L.; Segerberg, L. H.; Schmidt, R. P.; Turrell, R. C., and Roseman, E.: The Electroencephalogram in Subdural Hematoma, J. Neurosurg. **9**:588-598 (Nov.) 1952.

The findings in this series did not bear out entirely Williams and Reynell's [13] conclusion that the alpha rhythm is suppressed only in the presence of hematomas in the posterior regions of the head. Our findings suggest that it is more likely to be suppressed in these instances but that it can be suppressed also in the presence of anteriorly located hematomas. This is in agreement with the observations of Sullivan and co-workers,[8] but in disagreement, however, with the findings of Marsh and associates.[5] The reason for this might be the number of cases involved and the fact, pointed out by Friedlander,[7] that the exact extent of the hematoma is difficult to judge from burr holes. We were somewhat more fortunate, since in 11 of our cases craniotomy had been performed for removal of the membrane and in other instances multiple burr holes were placed.

Role of the Brain Stem in Producing Dysrhythmic Activity.—While suppression of alpha activity and the presence of focal slow activity have been frequently commented on in the Anglo-American literature, we did not find much emphasis on records with dysrhythmic activity, even though such activity is clearly visible in some of the illustrations in the literature (Figs. 3 and 4 of Cohn [9] and Fig. 8 of Marsh and co-workers [5]). The findings had been mentioned by Marsh and associates in their series and were also commented on by Paillas and Naquet,[14] who found dysrhythmia in 8 of 13 cases. The last two investigators concluded that the brain stem plays an important part in producing this dysrhythmia, and they also pointed out that this would explain the frequency of homolateral pyramidal signs.

In our series, 24 of 37 adolescents and adults showed dysrhythmic activity. We found paroxysmal and bilaterally synchronous discharges which gave the impression of a projected disturbance, as well as theta rhythms. Since these dysrhythmias were associated in all but three cases with a marked derangement in the patient's mental state, there seemed to be some connection between the two. Clinically, the most significant finding associated with subdural hematoma is the rapid change in the patient's mental status. He may be fully awake at one time and be comatose one or two hours later, or vice versa. This factor and the electroencephalographic findings are of interest in relation to the work of Lindsley and associates [15] on the activating system of the brain stem. These investigators showed that it is possible to obtain high-voltage slow waves from the cortex of cats after selective destruction of either the basal diencephalon or the tegmentum of the midbrain. It is possible, therefore, to postulate that these dysrhythmias may indicate an injury to the activating system of the brain stem. Another factor of interest in this connection is the observation that mental activity reduced the abnormal slow discharges in five cases. This can be regarded as an arousal phenomenon and may link with the experimental findings of Ingram and co-workers,[16] who demonstrated that the abnormal slow waves

13. Williams, D., and Reynell, J.: Abnormal Suppression of Cortical Frequencies, Brain **68**:123-161 (June) 1945.

14. Paillas, J. E., and Naquet, R.: Corrélations électro-anatomocliniques au cours des hématomes sous-duraux, Rev. neurol. **83**:602-608 (Dec. 6) 1950.

15. Lindsley, D. B.; Bowden, J. W., and Magoun, H. W.: Effect upon the EEG of Acute Injury to the Brain Stem Activating System, Electroencephalog. & Clin. Neurophysiol. **1**:475-486 (Nov.) 1949.

16. Ingram, W. R.; Knott, J. R.; Wheatley, M. D., and Summers, T. D.: Physiological Relationships Between Hypothalamus and Cerebral Cortex, Electroencephalog. & Clin. Neurophysiol. **3**:37-58 (Feb.) 1951.

produced by lesions in the posterior hypothalamus and the upper part of the midbrain in cats could be suppressed by arousal stimuli of sufficient intensity.

The same standard calculations brought about an "arousal" response in six cases; it failed to do so in four others. This may mean either that two different systems were affected or that the patients exhibited a different level of awareness.

With these questions in mind, the material on adolescents and adults was reviewed again from the clinical side to find possible additional evidence of damage to the brain stem. It was learned that of 19 cases of unilateral hematoma in which dysrhythmia was present there was x-ray evidence of marked displacement of the brain to the opposite side in 4, the pineal gland being shifted not only to the other side but also backward and downward. In three other cases pyramidal tract signs were present on the side of the subdural hematoma only. In five additional cases contralateral, as well as homolateral, reflex findings were presented, and in two cases there were symptoms referable to the homolateral third nerve (internal ophthalmoplegia in one and complete ophthalmoplegia in the other). In the remaining five cases there were, in addition to the altered mental state, only contralateral muscle findings.

A review of the 12 cases of unilateral hematoma in which the records showed no dysrhythmic activity revealed that in 10 there were only contralateral muscle findings or aphasia or no lateralizing findings at all, while in 2 instances there was x-ray evidence of displacement of the brain to the opposite side. From this evidence it is reasonable to assume that the brain stem does play a major role in explaining the clinical picture, as well as the electroencephalographic abnormalities.

The question arises as to why some of the subdural hematomas produced the picture of brain-stem involvement and others did not. The amount of the local accumulation of blood (up to 240 cc. was evacuated in some instances) and the resultant pressure exerted on the stem may be factors. In other cases, however, only 50 cc. of blood or less was in the subdural space, but the patient had experienced a severe head injury either by falling down stairs or by being involved in a car accident. In such incidents the coup and the contrecoup effects would also be on the vertex and on the base, with the possibility of damage to the reticular structures.

A third factor in producing the picture of brain-stem involvement may have been that the pressure exerted by a bilateral subdural hematoma could have resulted in displacement of the brain stem. Such a hematoma may be so massive that it produces the clinical picture of decerebrate rigidity. While this might explain some of the confusing findings, a number of other factors were probably at work in producing the apparent variety in the clinical and electroencephalographic pictures. It would be especially interesting to find out why patients can have more than 100 cc. of blood in one subdural space and yet still present an essentially normal electroencephalogram.

SUMMARY

The records of 45 cases of surgically proved subdural hematomas are reviewed. Eight of the patients were children less than 10 years of age, and the rest were adolescents and adults. In most of the cases the condition was chronic.

The most significant finding for the entire series was the occurrence of focal slow waves. Alpha rhythm or background asymmetry was present in only 48.1%.

The electroencephalogram was less helpful in diagnosis in the childhood group than in the adolescent and adult group.

Suppression of alpha rhythm was associated not only with posteriorly located hematomas but also with anterior ones.

The response to photic stimulation (driving response) was not a reliable index to lateralization.

It is pointed out that differences of amplitude can lead to wrong lateralizations in cases in which a subdural hematoma cannot be suspected either from the clinical history or from the electroencephalographic findings.

The occurrence of dysrhythmic components in the recording is observed and discussed in relation to the role the brain stem may play in the production of these findings. The relation of neurologic to electroencephalographic findings is brought out. The results seem to indicate that the majority of the dysrhythmias were due to damage of the brain stem.

WILSON'S DISEASE (HEPATOLENTICULAR DISEASE)

A Family Study

FRANK L. SULLIVAN, M.D.
HERBERT L. MARTIN, M.D.
AND
FLETCHER McDOWELL, M.D.
NEW YORK

CURRAN,[1] at Bellevue Hospital, in 1931 described a family in which five of six siblings had Strümpell-Westphal pseudosclerosis, or progressive hepatolenticular degeneration. Readmission of two of these siblings in 1952 presented us with an opportunity to study again and to review an unusually large family group with this disorder and to observe the natural history of the disease during a 21-year period. Wilson,[2] in his discussion of hepatolenticular degeneration, noted only one family with more members afflicted, a family of 14 in which 6 members had the disease. He reported only two patients who lived more than 20 years after the onset of symptoms. One patient lived 41 years, and another was alive at the time of the report, 28 years after the appearance of symptoms.

The clinical evidence for the familial nature of this disease is well established.[2] Recent family studies have indicated that even the members of the family who show no clinical evidence of hepatolenticular degeneration may show some characteristic biochemical dysfunction, notably a nonspecific amino-aciduria.[3]

It is the purpose of this paper to extend the histories first presented by Curran and to describe recent studies of the four remaining members of the family.

REPORT ON FAMILY

In the Figure is shown the genealogical chart of the family. Three of the four generations about which we have information were born in Russia, of Jewish extraction. There has been no history of neurological disorder prior to the present generation. The parents of this generation were first cousins and came to this country in the early part of the century. They were married in 1908 and have since resided in New York.

The father died at the age of 37, of pemphigus, and a paternal aunt is known to have active pulmonary and articular tuberculosis. A paternal uncle is in good health.

The maternal relatives give a history of death due to infectious diseases, including measles, pneumonia, and typhus. Two maternal aunts are in good health at the present time. The mother, who is 61, has no neurological or visceral indication of hepatolenticular degeneration. She has had three miscarriages and seven full-term live births.

From the Second Cornell Medical (Neurology) Division, Bellevue Hospital, and the Department of Medicine, Cornell University Medical College.

1. Curran, F. J.: Pseudosclerosis of Strümpell-Westphal in 5 Members of a Family, J. Neurol. & Psychopath. **12**:320, 1952.

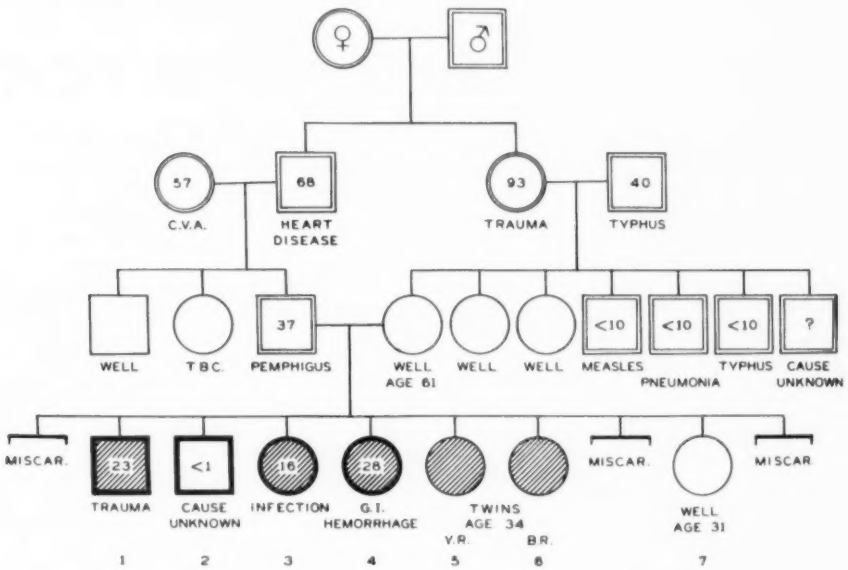
2. Wilson, S. A. K.: Neurology, edited by A. N. Bruce, Baltimore, William Wood & Company, 1940, Vol. 2, pp. 806-831.

3. Uzman, L. L., and Hood, B.: The Familial Nature of the Amino-Aciduria of Wilson's Disease (Hepatolenticular Degeneration), Am. J. M. Sc. **223**:392, 1952.

The first child, a boy, was well until the age of 13, when, after head trauma, he was unconscious for two hours. At the age of 16 he had a motility disorder diagnosed as chorea and two years later exhibited generalized retardation of movements, slurred speech, and abnormal behavior, characterized by emotional lability, irritability, and mental retardation. He was hospitalized by the state because of these symptoms. Two years before his death he had onset of a seizure disorder. At that time he was seen at Bellevue Hospital, where bilateral Kayser-Fleischer rings were noted, in addition to mask-like facies, dysarthria, inability to perform rapid rhythmic alternating movements, and intention tremor of the left hand. Skilled acts were poorly performed. The results of liver function tests were within normal limits.

The patient refused to undergo further diagnostic procedures and, because of his marked personality and behavior disorder, was transferred to a psychiatric institution, where he died two years later, at the age of 23, after an accidental cervical fracture.

The second child died in infancy, of an unknown cause.



Genealogical tree of family with hepatolenticular disease.

The third child, a girl, was noted to have tremor in the right hand at the age of 13, followed two years later by tremor in the left hand and generalized weakness. On examination, she presented bilateral Kayser-Fleischer rings, slurring of speech, and marked intention tremor of all extremities. At the age of 13 her intelligence quotient on the Stanford-Binet scale was reported to be 103, but two years later it was found to be 73. The findings on clinical laboratory examinations, including liver function tests, were within normal limits. She exhibited emotional lability, with wide mood swings, lying, suicidal threats, and precocious sexual behavior. Therefore she was transferred to the psychiatric division of Bellevue Hospital, where she died a year later, of a throat infection.

The fourth child, a girl, at the age of 7 years was jaundiced and had an enlarged liver. Drowsiness and tremor, presented at the age of 14, were thought to be evidence of encephalitis lethargica. At the age of 15 she had tremor of the hands, slurring of speech, and difficulty in swallowing. These symptoms progressed, so that two years later hospitalization was necessary. Examination showed euphoria, bilateral Kayser-Fleischer rings, a positive Romberg sign, staggering gait, intention tremor, motor incoordination, and hyperactive deep reflexes. The liver was

not palpable, and the results of liver function studies were within normal limits. During her 12-year hospitalization the patient's disease continued a relentless downhill course, with both physical and mental deterioration and several short episodes of hepatic coma. At the age of 28 she had a protracted episode of hematemesis and died.

The fifth and sixth children, Y. R. and B. R., are female twins, showing objective evidence of being identical. The onset, course, and present state of their illness have been remarkably similar.

Y. R. is now 34 years of age and is known to have had bilateral Kayser-Fleischer rings, slurred speech, intention tremor, and poorly coordinated movements for at least 21 years. Since she was first examined, at the age of 13, she has completed elementary school and attended business school for a short time but has never been employable. She married at the age of 26 but was unable to care for her household because of her motility disorder.

Since her separation from her husband, six years ago, she has noted progressive difficulty in caring for herself and has required increasing help from her mother and stepfather. At the time of her recent hospital admission she was unable to walk, feed herself, or care for her person and was incontinent of urine and feces. On examination a well-defined Kayser-Fleischer ring was shown bilaterally, and the liver edge was palpable 2 to 3 cm. below the right costal margin and was not tender. She exhibited inappropriate behavior, characterized by childishness, a coy, evasive manner, and eroticism. She was oriented as to time, place, and person and showed no delusions or hallucinations; her memory was intact. There was generalized weakness of all muscles in the upper and lower extremities, and resistance to passive movement was increased, on the left more than on the right. There was severe impairment of function in point-to-point tests, and rapid rhythmic alternating movements were uncoordinated and slowly performed. An involuntary tremor of both hands was most noticeable on movement, but was present also at rest. Deep reflexes were hyperactive throughout; the ankle clonus was elicited bilaterally, but the plantar response was of flexor type. There was no demonstrable loss of sensation. The results of routine laboratory examination were normal, but the cephalin flocculation reading was persistently 2+; the sulfobromophthalein retention was 20% in 45 minutes, and serum cholesterol ranged from 312 to 410 mg. per 100 cc., with normal esters. A Stanford-Binet intelligence quotient was 116 at the age of 13, while on the present admission, at the age of 34, a Bellevue-Wechsler intelligence score was 82, thus indicating serious impairment of mentation. The electroencephalogram showed a nonspecific pathological record. Biopsy of the liver revealed normal structure.

B. R. was found at the age of 13 to have bilateral Kayser-Fleischer rings, intention tremor, and staggering gait. At the age of 17 she married a man 10 years her senior but was never able to care for her household.

At the age of 32, during a period of emotional upheaval, she noted increasing tremor of her hand and unsteadiness of gait. Examination revealed bilateral Kayser-Fleischer rings, emotional lability with sudden outbursts of laughter, unsteady gait, a nasal quality of the voice, slight rotatory tremor of the head, poor performance in the point-to-point test, and impairment of rapid rhythmic alternating movements in the arms and legs. Deep reflexes were equal and active throughout, but resistance to passive movement was generally increased. Sensation was intact. The cephalin flocculation reading was 2+; the thymol turbidity test gave a 4+ reaction, and alkaline phosphatase measured 8.6 Bodansky units. The cerebrospinal fluid protein was 60 mg. per 100 cc. Clinical laboratory examinations were otherwise within normal limits. The electroencephalogram showed nonspecific abnormality. Biopsy of the liver showed normal structure.

The seventh child, a woman, aged 31 at the time of writing, has exhibited limited intelligence, symptoms of a serious personality disorder, and social maladjustment since childhood. She has, however, never presented defects of the nervous system or corneal pigmentation characteristic of hepatolenticular degeneration.

Table 1 summarizes the evidence of biochemical dysfunction in the twins, Y. R. and B. R. Both patients exhibit a low serum ceruloplasmin [4] concentration, as compared with a normal of

4. Ceruloplasmin is a blue α-globulin containing 0.34% copper, or eight atoms of copper per molecule. It represents approximately 0.5% of plasma protein. Scheinberg, I. H., and Gitlin, D.: Deficiency of Ceruloplasmin in Patients with Hepatolenticular Degeneration, Science **116**: 484, 1952.

30 mg. per 100 ml.; a low serum copper concentration, as compared with a normal of 120 to 160 γ per 100 ml.; an elevated urinary copper output per 24 hours, as compared with a normal of 30 to 60 γ, and an elevated urinary α-amino-acid nitrogen excretion per 24 hours, as compared with a normal of 160 to 200 mg. per liter.

Abnormalities similar to those found in the twins were sought for in the mother and the sister, who showed no clinical evidence of hepatolenticular degeneration. Although familial biochemical dysfunction has been reported, Table 2 demonstrates that values for serum copper, urinary copper excretion, and urinary α-amino-acid nitrogen excretion for the mother and sister do not show the aberrations associated with this disorder. The mother exhibits a somewhat elevated urinary copper excretion; this abnormality, however, is seen in other disease states. A low serum copper concentration is the more constantly encountered biochemical abnormality.[5]

It is interesting to note that clinical improvement in motility function in the two patients with hepatolenticular degeneration has followed the administration of dimercaprol U. S. P. (BAL). Improvement has been greatest in Y. R., who has been treated for seven months. She was bed-

TABLE 1.—*Biochemical Data on Y. R. and B. R.*

	Cerulo-plasmin, Mg./100 Cc.	Serum Copper, γ/100 Cc.	Urinary Copper Excretion, γ/24 Hr.	Urinary α-Amino-Acid Nitrogen Excretion, Mg./24 Hr.
Normal	30	120-160	30-60	160-200
Y. R.	4	45	623	845
B. R.	7	43	625	952

TABLE 2.—*Biochemical Data on Twins Y. R. and B. R. and on Their Mother and Sister*

Subject	Serum Copper Concentration, γ/100 Cc.	Urinary Copper Excretion, γ/L.	Urinary α-Amino-Acid N. Excretion, Mg./L.
Normal	120-160	30-60	164-204
Y. R.	45	318	432
B. R.	43	438	669
F. W. (sister)	161	112	178
A. W. (mother)	260	235	77

ridden and incontinent of urine and feces at the time treatment began; now she is ambulatory and able to care for herself. B. R., after 10 days of treatment 2 months ago, can now walk more steadily and shows less intention tremor and fewer adventitious movements.

SUMMARY

We present the natural history of a family of seven children, of whom five, including one pair of twins, have had progressive hepatolenticular degeneration. The case histories of two of the patients, still living 21 years after the onset of symptoms and presenting what is both clinical and biochemical evidence of this disorder, are reported in detail, in the nature of a follow-up of the paper by Curran, in 1931. The twins exhibit characteristic low serum copper concentration and ceruloplasmin content, but no such abnormality can be demonstrated in the unaffected members of the family.

Dr. Alexander G. Bearn, of the Rockefeller Institute for Medical Research, and Dr. I. Herbert Scheinberg, of the Harvard Medical School, cooperated in obtaining the biochemical data reported in this presentation.

5. Bearn, A. G.: Personal communication to the authors.

Case Reports

PHOTOGENIC EPILEPSY: PARAMETERS OF ACTIVATION

C. MARSHALL, M.D.
A. EARL WALKER, M.D.
AND
S. LIVINGSTON, M.D.
BALTIMORE

AS MUCH of the recent investigation into the field of activation of the electroencephalogram by intermittent photic stimulation has been of purely scientific nature,[1] an account of a more practical application of the technique to the clinical problems of epilepsy seems appropriate.

REPORT OF CASE

History.—J. G. a white farmer aged 31, since the age of 10 years had suffered from major convulsive seizures; these had gradually increased in severity and frequency until they numbered 10 to 12 a year. The patient had noted no aura or warning while he was conscious.

The attacks, all preceded by exposure to bright or flickering light, consisted of a sudden loss of consciousness without warning, falling to the ground, and rolling up of the eyes, followed by generalized tonic and clonic convulsions. The average duration of such a seizure was 15 to 20 minutes. During seizures the patient had bitten his tongue, injured his lips, and fractured his jaw. Occasionally, at the beginning of a seizure, he would involuntarily bring his left hand before his eyes, a movement which he was able to control, at times, with great effort. The patient had learned that whenever he was exhausted, tense, or nervous he was more likely to have an attack. He had been treated by one of us (S. L.) with phenobarbital, bromides, and diphenylhydantoin (Dilantin), with some improvement.

No abnormalities were found on physical, ophthalmological, or neurological examination except for scars on the chin and tongue. The results of urinalyses and blood examinations were reported as normal. The photogenic attacks were studied in detail with a view to determining the parameters of excitation.

Equipment and Methods of Investigation.—The source of the intermittent light consisted of a General Radio Strobolux fired by a wave shaper designed by one of us (C. M.), which was, in turn, driven by a Hewlett-Packard Model 202D sine-wave oscillator. Continuously variable attenuations of the light intensity were obtained by placing, on the subject, a pair of glasses with Polaroid lenses oriented in parallel planes; a large rotable disk of Polaroid, mounted before the glasses, permitted identical bilateral control of intensity. Attenuation was measured with an incandescent light source by means of a Weston Master II light meter; the disk rotation was calibrated in percentage attenuation as compared with the unobstructed light. The two Polaroid

This paper was presented at a meeting of the Eastern Association of Electroencephalographers, March 17, 1951.

From the Division of Neurological Surgery (Drs. Marshall and Walker), and the Department of Pediatrics (Dr. Livingstone), The Johns Hopkins University School of Medicine.

1. Hill, J. D. N., and Parr, G., Editors: Electroencephalography: A Symposium of Its Various Aspects, London, Macdonald & Co. (Publishers), Ltd., 1950.

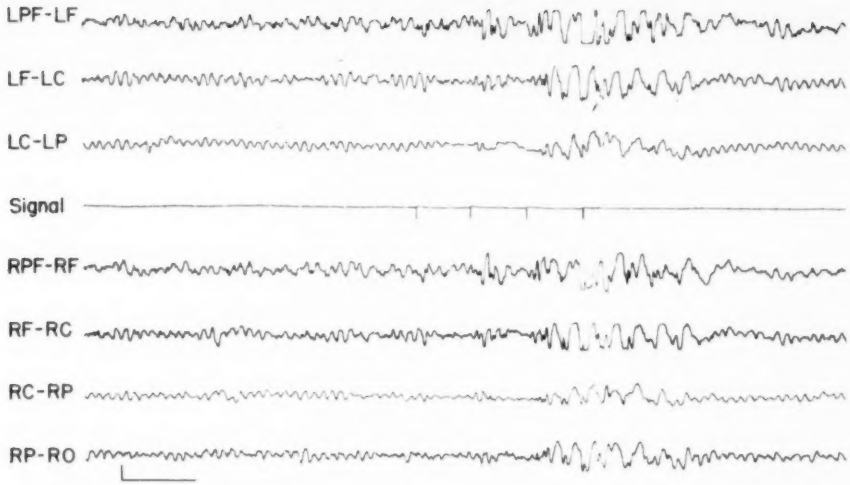


Fig. 1.—Electroencephalogram showing a pronounced reaction to four bright flashes of light. As in all the illustrations, the horizontal line represents an interval of one second; the vertical line, a signal of 50 μv.

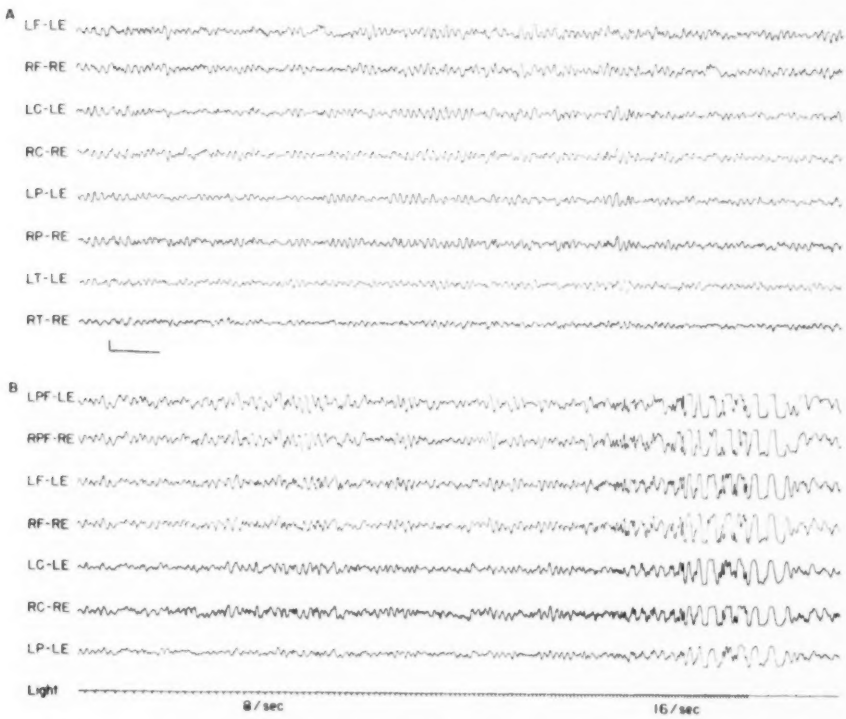


Fig. 2.—*A*, spontaneous record. *B*, effects of low-intensity photic stimulation. There occur an increase of voltage when the flash frequency reaches 8 cps and a further increase when it reaches 16 cps.

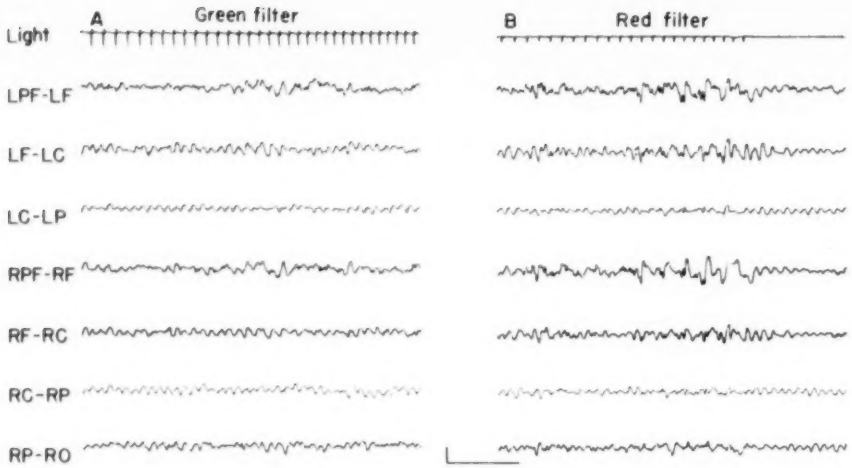


Fig. 3.—*A*, effect on the electroencephalogram of passing the light through a green filter. *B*, effect of passing the light through a red filter. The light intensity in *A* was tenfold that in *B* even after compensation for the total intensity variations due to the filters.

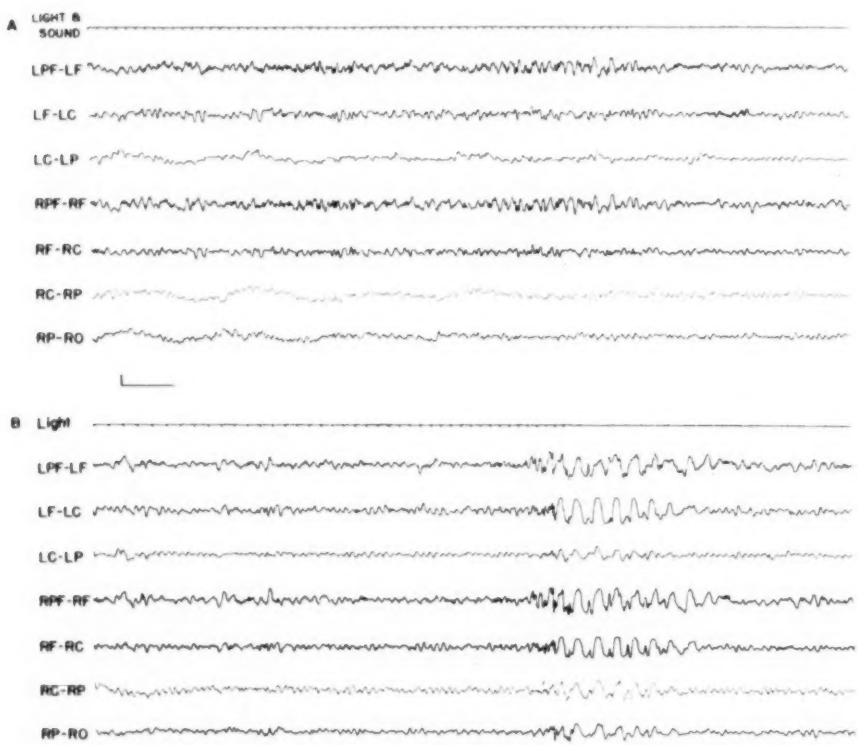


Fig. 4.—*A*, effect on the electroencephalogram of coupling each flash of light with a loud "click," which follows the flash by 1 msec. *B*, effect of the light without sound; all other factors were unchanged.

sheets with mountings, when in phase, gave a 90% attenuation; this attenuation reached 99.6% when the planes were 90 degrees out of phase. Auditory stimulation was produced by discharging a 4-mfd. condenser charged to 300 volts into the 8-ohm voice coil of a speaker placed 1 ft. (30 cm.) above the patient's vertex. As the firing was accomplished electronically in synchrony with the light trigger, the time delay occasioned by the sound traveling from speaker to ears was approximately 1 msec.; this made it fall after the light flash, which lasted approximately 50 μsec. With the patient supine, the light housing was placed within 2 in. (5 cm.) of his nose so as to fill as much of the visual fields as possible.

As the precipitation of a convulsion would have temporarily put an end to the investigation, subthreshold stimulation was used as far as possible. The lowest intensity step on the Strobolux was found to be epileptogenic if the time and frequency of stimulation were adequate. This minimal light source, the absolute light intensity measurement of which was not made, was used for the experimentation. First, the patient's sensitivity to various frequencies from 2 to 20 cps at different levels of light intensity was investigated. Second, at the optimum frequencies (8 and 16 cps) further and more precise intensity measurements were made with varying colors from relatively sharp-cutting photographic filters (Wratten filters A, B, C5).

The criterion for a positive reaction to the light was decided upon after the precipitation of four generalized convulsions. In earlier investigations, the appearance of high-voltage slow waves or spike-and-dome complexes was looked upon as positive. Later, however, it became apparent that the appearance of moderate-voltage dysrhythmia was almost invariably followed by the spike-and-wave pattern, which would progress to a generalized clinical convulsion if stimulation was continued. Accordingly, in the later experiments, the induction of a dysrhythmia alone was considered indicative of a positive reaction.

Observations.—With this very cooperative patient, on a total of six occasions a great number of observations were made. Though some of the results were only verifications of findings reported by other workers, the simplicity and clarity of the recordings were gratifying. While the patient's threshold remained satisfactorily constant during any one recording period, there was a definite variation of threshold from one period to another, usually days apart.

1. Frequency: When frequency was plotted against light intensity, it was found that with high intensity the patient would react to any frequency from 2 to 20 cps (Fig. 1). However, as the brightness was decreased, certain critical frequencies made themselves apparent; at the lowest intensity which would give any reaction, this reaction appeared at 8 and 16 cps (Fig. 2). As the brightness was increased, the frequency range capable of giving a reaction spread both upward and downward from these two points.

With one eye covered, the light intensity had to be approximately doubled in order that stimulation should reach threshold. In addition to this, with unilateral stimulation, the patient seemed able to inhibit or suppress the progression of a seizure from a marked disorganization of the electroencephalogram, a compensating mechanism not seen with bilateral stimulation.

2. Wave Length: An analysis was made of the effect of colors, using red, green, and blue. A multitude of factors, such as the color temperature of the light source, the filter spectra, the color sensitivity curve of the eye, the filter effect of the eyelids, and the light-meter color curve complicated the calculations of intensity. However, after all these factors had been considered, an increased sensitivity to red by a factor of 10 was observed (Fig. 3).

3. Auditory Stimuli: If, during threshold stimulation—one just high enough to elicit repeatedly high-voltage slow waves with spikes—a loud click was introduced about 1 msec. after the light flash, only moderate dysrhythmia resulted, without its proceeding to the seizure pattern (Fig. 4). With increase of light intensity by a factor of 4 the inhibiting effect of the sound was overcome. Other means of peripheral stimulation—mild peripheral electric shock, sufficient to cause discomfort, and a blood pressure cuff around the upper arm—failed to reproduce this inhibiting effect.

4. Effect of Drugs: Using this same method of finding a threshold and then varying some one factor, we tried the effect of amphetamine (10 mg. given orally) and phenobarbital (4 grains 0.25 gm.), injected intravenously. Neither showed any positive shift of threshold.

On the basis of these findings, green glasses, to approximate the B, or green, filter, were prescribed. When worn, these seemed to decrease the attacks, and minus red glasses, prescribed later, eliminated the seizures. When the patient had these glasses on, his threshold for a positive reaction was 10 times the intensity of light which would give a response with a neutral density filter of the same attenuation factor (Fig. 5).

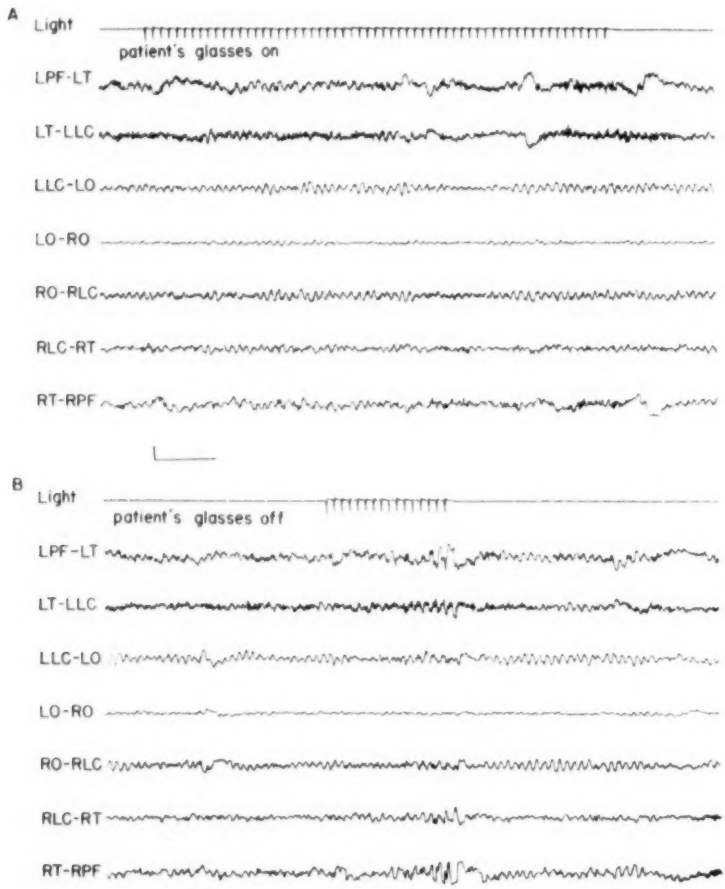


Fig. 5.—*A*, absence of effect on the record when the patient viewed the light through minus red glasses. *B*, effect without glasses of stimulus after the light intensity had been attenuated to compensate for the total light attenuation of the glasses plus an additional tenfold attenuation.

COMMENT

Sensory stimuli-precipitated seizures have been known for many years, but few electroencephalographic studies have been made. The resemblance of photic driving to epileptic activity was pointed out in 1944 (Walker, Woolf, Halstead, and Case [2]),

2. Walker, A. E.; Woolf, J. I.; Halstead, W. C., and Case, T. J.: Photic Driving, Arch. Neurol. & Psychiat. **52**:117-125, 1944.

and this observation stimulated Cobb[3] to report on three cases in which photic stimulation seemed to precipitate the attacks. These observations were forgotten because techniques for photic stimulation at that time employed a light source too feeble for effective activation. It was the introduction by Rémond and Gastaut[4] of the activation technique of pentylenetetrazol (Metrazol) and photic stimulation which led to general interest in the subject.

The mechanism by which sensory impulses trigger convulsive activity are poorly understood in spite of considerable, though conflicting, research. This report does not clarify the mechanism. It merely indicates that certain parameters of stimulation are particularly effective in inducing the response. That frequencies of the alpha range and its harmonies are particularly effective might suggest that a cumulative, or hypersynchronic, interlocking of the spontaneous and induced responses occurs. Bartley's observation that brightness is enhanced by flickering at the alpha frequency may be similarly related. The mechanism by which the red end of the spectrum is so effective in triggering an attack of photogenic epilepsy is even less well understood. There is no evidence that the red frequencies have a sharper retinal range than the other frequencies and hence cause a more synchronous response in the geniculate body and striate cortex. Nor is the dark-adapted eye more sensitive to the red end of the spectrum. The sensitivity would therefore seem to be due to the integration of the red-carrying elements, probably at the geniculate level and secondarily at the cortical level. However, we have no evidence at this time of the anatomical or physiological peculiarities of this system.

It was interesting to note that the patient denied having an aura to his attacks, and yet after we had informed him of several photically induced encephalographic "aura," he admitted to having an indescribable, but characteristic, sensation just prior to the beginning of the electroencephalographic changes. Further exploration made it apparent that this sensation was coincident with the beginning of the disorganization of the alpha rhythm. The aura remained the same irrespective of the degree of the disorganization of the brain waves. The failure to recognize an aura in the spontaneous attacks can probably be correlated with the amnesia for events preceding the actual attack which usually occurs.

SUMMARY

By use of intensity attenuation of a stroboscope light with Polaroid filters, and by noting the amount of light required to give a positive electroencephalographic reaction of increased voltage with slowing, it was demonstrated that red light was at least 10 times as effective in triggering attacks in a case of photogenic epilepsy as were other colored lights tried. Minus red glasses were of considerable aid to the patient.

3. Cobb, S.: Photic Driving as a Cause of Clinical Seizures in Epileptic Patients, Arch. Neurol. & Psychiat. **58**:70-71, 1947.

4. Rémond, A., and Gastaut, H.: L'"epitest" ou l'activation chimico-physique dans l'étude et le diagnostic de l'épilepsie, Rev. neurol. **81**:503-506, 1949.

MARCH OF PILOERECTION AS A CONVULSIVE EQUIVALENT

WILLIAM M. LANDAU, M.D.
ST. LOUIS

THE PRINCIPAL evidence that the human cortex exercises a control over visceral functions is derived from cases presenting destructive lesions of cortical efferent tracts.[1] Piloerection, among other autonomic responses, may be willed, directly or indirectly, an observation also suggesting that the cortex is somehow involved.[2] Experimentally, piloerection has been obtained by stimulating the cingulate cortex of the monkey [3]; a path descending from the cingulum through the tegmentum may be presumed to convey the activity to lower autonomic centers (Brown and Sherrington [4]; Walker [5]).

Féré [6] reported a case of localized piloerection on the face, sometimes associated with unilateral focal convulsion. This phenomenon occurred in a patient who also had attacks of migraine and of a generalized seizure. Generalized piloerection associated with convulsion was described in a case by Féré [7] and in other cases by Hutchinson.[8] Bucy and Pribram [9] noted focal sweating as one incident of cortical discharge and reviewed the pertinent literature.

The case described here is unusual because of the march of piloerection and the accompanying psychical phenomena.

REPORT OF A CASE

J. G. K., a salesman aged 29, was well prior to enlisting in the Army in 1942, at the age of 19. His medical history was noncontributory, and there was no familial history of convulsive

From the Section of Neurology, Washington University School of Medicine.

1. (*a*) Kennard, M.: Autonomic Functions, in Bucy, P. C., Editor: The Precentral Motor Cortex, Urbana, Ill., University of Illinois Press, 1944, pp. 293-306. (*b*) Brickner, R. M.: Certain Characteristics of the Cortical Influence over the Sympathetic Nervous System in Man, J. Nerv. & Ment. Dis. **71**:689-713, 1930.

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3. Hoff, E. C., and Green, H. D.: Cardiovascular Reactions Induced by Electrical Stimulation of the Cerebral Cortex, Am. J. Physiol. **117**:411-422, 1936. Smith, W. K.: Functional Significance of the Rostral Cingular Cortex as Revealed by Its Responses to Electrical Excitation, J. Neurophysiol. **8**:241-255, 1945.

4. Brown, T. G., and Sherrington, C. S.: Notes on the Pilomotor System, Quart. J. Exper. Physiol. **4**:193-205, 1911.

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6. Féré, C.: Horripilation unilatérale paroxystique, Compt. rend. Soc. biol. **56**:546-547, 1904.

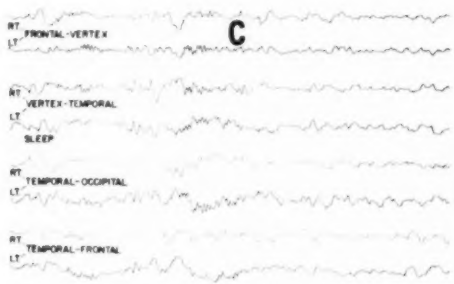
7. Féré, C.: Note sur un cas d'epilepsie affectant principalement le système nerveux de la vie organique, Compt. rend. Soc. biol. **48**:1034-1036, 1896.

8. Hutchinson, J.: Additional Notes on Horripilatio, J. Hutchinson's Arch. Surg. **9**:132-136, 1898.

9. Bucy, P. C., and Pribram, K. H.: Localized Sweating as Part of a Localized Convulsive Seizure, Arch. Neurol. & Psychiat. **50**:456-461, 1943.

disorder, migraine, or other neurological disease. In 1943 there developed cellulitis of the right shoulder, with formation of an abscess over the course of a week. Then hyperpyrexia developed suddenly, he became irrational, and was semicomatose for the next two weeks. Green-producing (alpha) and hemolytic (beta) streptococci were cultured from the abscess. He was treated with sulfonamide drugs and drainage and was returned to duty after 117 days of hospitalization.

He had his first minor seizure in 1945, and these attacks have continued to recur at intervals of a few minutes to a month. A disturbed emotional state precedes the occurrence of some of them. During a typical attack he is reported to appear pale and shaky. There is no identifiable aura, but he does experience a fading-away of sounds and an associated feeling of strangeness, sadness, fear, and unreality. He may feel simultaneously that he has had a spell previously under the same circumstances. As the psychical phenomena develop, a prickly, cold sensation is felt behind the right ear. Piloerection and goose flesh then appear in the area and spread over the right side of the face and neck, the cold sensation following in its wake. An involuntary shudder



A, resting electroencephalographic record with one burst of 6 cps. activity; *B*, exaggeration of dysrhythmia by hyperventilation; *C*, right anterocentral focal trend during sleep.

of the right shoulder may occur as the sensation reaches it. The piloerection and cold sensation descend the right arm and forearm, thereafter becoming evident in the right leg, apparently skipping the trunk. The right nostril sometimes becomes blocked with serous discharge during a seizure. However, no lateralized lacrimal, sudomotor, or vasomotor activity has been observed. An entire seizure lasts 20 to 60 seconds. There is no loss of consciousness or evidence of sensorimotor deficit. He can talk during an attack and has written a coherent description of the sensations as they develop. If he feels depressed during a seizure, he may weep, and often prays.

In 1947 the patient began to have generalized convulsions, in addition to the minor seizures. These have always occurred during sleep, with a maximum frequency of two to three a month. Recently they have been controlled successfully by anticonvulsant drugs.

The physical condition was unremarkable. The patient was right-handed. There was a fixed scar over the right deltoid. The blood pressure was 126/66. The pupils were round and equal and responded actively in accommodation and to light and painful stimuli. The fundi were normal, and the central and peripheral visual fields were full. Motor, sensory, and reflex exami-

nations showed a normal condition. The pilomotor reflex-[11b] was symmetrical and of normal intensity. No abnormal symptoms were produced by five minutes of hyperventilation. The mental status was not unusual. He had apparently adjusted well since his discharge from the Army, was married, and had two children. A psychological examination showed no evidence of organic deficit or of unusual thought processes.

No abnormalities were noted in a pneumoencephalogram made in 1947. Several electroencephalograms were recorded (Figure). Resting records showed occasional bursts of 6 cps activity, which was exaggerated in amplitude by hyperventilation. Some asynchrony was noted occasionally in the central lead combinations, but no clearly focal or lateralized process was recorded. During a sleep tracing the left-right asynchrony was more constant, a suggestion of slow focal activity appearing at the right temporal lead. No paroxysmal sequence appeared during the sleep recording.

The seizures have been observed by several independent watchers, but it has been impossible to obtain coincident electroencephalographic recordings and observations on autonomic functions during one of them.

COMMENT

That piloerection is a minor-seizure manifestation in this case is inferred from the occurrence of march and the coincidence of generalized seizures; focal cerebral infection incident to streptococcic septicemia has a possible etiological significance. The absence of abnormal findings in air studies, the normal visual fields, and a relatively nonfocal electroencephalogram are evidence against a structural lesion. The psychical concomitants of the minor seizures appear to place the disordered process in the temporal lobe, but whether the cortical area whose discharge produces piloerection is coextensive with, neighboring upon, or remote from that initiating the psychical phenomena is not clear. However, the near simultaneity in time of development suggests a close areal relation. From the pattern of march a localization akin to the somatotopic may be inferred, and the accompanying psychical phenomena suggest a cortical origin for the piloerection. Thus, though localization has been shown for somatic activity in the nonpyramidal paths,[10] it seems more likely that the march of piloerection is mediated over the pyramidal tract in this case. The autonomic responses to unilateral pyramidal stimulation in experimental animals occur bilaterally[11]; therefore, a right-sided autonomic seizure pattern is not inconsistent with the equivocal right central electroencephalographic lateralization.

It is not inferred that piloerection has an isolated cortical representation,[12] even though it may originate focally as a manifestation of a seizure process. The mechanism probably is more complex, such rare cases as the one presented emphasizing but one facet of piloerector control.

SUMMARY

A case is described in which, in addition to generalized motor seizures, there occurred minor ones, characterized by subjective feelings of unreality, distance, and déjà vu, and by a march of piloerection over one side of the body.

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11. Landau, W. M.: Autonomic Responses Mediated via the Corticospinal Tract, J. Neurophysiol, to be published.

12. Denny-Brown, D. E.: The Frontal Lobes and Their Functions, in Feiling, A., Editor: Modern Trends in Neurology, New York, Paul B. Hoeber, Inc., 1951, pp. 13-89.

Society Transactions

CHICAGO NEUROLOGICAL SOCIETY

Harold C. Voris, M.D., *President in the Chair*
Regular Meeting, Dec. 9, 1952

Acanthocytosis: A New Hematologic-Neurologic Syndrome. Dr. M. A. Perlstein and Dr. K. Singer.

Acanthocytosis is a hereditary, recessively transmitted disease characterized by an atypical spiculated appearance of the erythrocytes (acanthocytes) and by a progressive neuropathy involving the dorsal columns, the cerebellar tracts, and the basal nuclei. To date, only two cases have been reported; both patients were of Jewish origin with consanguineous parents. They had had a celiac syndrome in infancy and presented evidence of vitamin-B deficiency.

A moving picture demonstrated the clinical aspects of the case of a boy aged 10 years.

DISCUSSION

Dr. Irving C. Sherman: Did you ever see this blood picture with other types of neurologic disease?

Dr. M. A. Perlstein: The blood picture precedes the neurologic changes. This child had been seen at the Mayo Clinic at the age of 2 years and followed there until he was 10 years of age. Crenated blood cells were reported in the blood smears; they were obviously similar to those we found. There were blood changes but no neurologic signs in the younger sibling of the patient reported by Bassini and Kornzweig.

Dr. Irving C. Sherman: Are there other cases in which these blood changes occur but neurologic symptoms do not develop after a long observation?

Dr. Harold C. Voris: What was the outcome in the other reported case?

Dr. M. A. Perlstein: The patient was still living when the report was made, two years ago. I do not know the eventual outcome.

Dr. Douglas N. Buchanan: I think I saw this boy between his visits to the Mayo Clinic. Was there any acid in the stomach?

Dr. M. A. Perlstein: Though he had no free acid, he had combined acid.

The Thymus and Its Relationship to Diseases of the Nervous System. Dr. Lee M. Eaton, Dr. O. Theron Clagett, and Dr. James A. Bastron, Rochester, Minn.

The pathologic, physiologic, and clinical evidences of the relation of the thymus to myasthenia gravis were reviewed.

The pathologic evidence is established by two factors: 1. The number of thymomas encountered in cases of myasthenia gravis (15%) cannot be explained by coincidence. 2. Lymphoid hyperplasia with formation of lymphoid germinal centers in the medulla is applicable to the non-neoplastic thymus of myasthenia gravis, rather than the concept of "persistence" and "hypertrophy" entertained by pathologists of the prethymectomy era.

The physiologic evidence of the relation of myasthenia gravis to the thymus is vague and contradictory and as yet has not been established.

Clinical evidence, particularly the results of surgical removal of the thymus, establishes this relationship with reasonable certainty. A study of 374 patients who had myasthenia gravis was reviewed. The results in 96 patients submitting to operation for removal of thymoma or thymus or both were compared with the results in the nonsurgical group.

DISCUSSION

DR. PAUL C. BUCY: Would Dr. Eaton explain what he means by complete remission?

DR. LEE M. EATON, Rochester, Minn.: By complete remission we mean that the patient feels he has completely recovered from myasthenia gravis and is taking no medicine known to relieve this condition. When the evaluation was made by letter, we accepted the information as evidence of complete remission. However, when we had a chance to reexamine the patients, we found minimal, but definite, evidence of myasthenia gravis in some, even though they felt they had completely recovered. Such patients were classified as showing ++++ improvement, or considerable improvement. Other patients showed no evidence of myasthenia gravis on examination until curare was administered. Occasionally the patient was definitely sensitive to curare. The disease was then not considered to be in complete remission, but the status was classified as that of considerable improvement.

DR. JOSEPH A. LUHAN: Am I correct in understanding that the results of removal of a persistent thymus were better than the results of removal of a gross tumor? By "no tumor," did the authors mean no roentgenographic evidence of tumor? Was a persistent thymus found at operation in all cases in which it was suspected?

DR. LEE M. EATON, Rochester, Minn.: In only one case did operation fail to show a significant amount of thymic tissue. In one case, that of an elderly man who was thought to have roentgenologic evidence of a thymic tumor, exploration revealed no tumor. The thymic fat was resected, but histologically a minimal amount of thymic tissue was present.

Dr. Good and his colleagues in the section on roentgenology of the Mayo Clinic have been very accurate in the diagnosis of thymic tumors. We have found them wrong in only 3 of approximately 430 cases. In one case the tumor in which they thought a tumor was present, it could not be found at exploration. In two cases in which the roentgenologist found no evidence of a thymic tumor, a small thymic tumor was found at exploration.

We found that it was difficult to compare the amount of thymic tissue by weighing the amount of tissue removed at the time of thymectomy. For instance, two patients might have 30 gm. of tissue removed at operation. Histologic study of the tissue might show that in one case over 90% was thymic tissue, whereas in another only 10% was thymic tissue, the rest being fat.

We believe that an incidence of 15% for thymic tumors in myasthenia gravis is approximately correct. Sir Geoffrey Keynes has found 11.6% of thymomas in his series.

DR. JOSEPH A. LUHAN: What was the course of the myasthenia gravis in the patients who had tumors revealed by x-ray?

DR. LEE M. EATON, Rochester, Minn.: There was insufficient time for the discussion of this problem in any detail. It can be said, however, that the patients with thymoma and the patients undergoing simple thymectomy differ in several ways. One important difference pertains to the age of onset. The average age of onset of myasthenia gravis in the tumor group was over 20 years later than the average age of onset in the patients who had simple thymectomy. For many of the patients who had thymoma operation could not be successful because of the malignancy of the thymoma. The greater risk of operation in cases of tumor is reflected by the incidence of 5 operative deaths among 41 patients with thymoma and only 3 operative deaths among 55 patients who did not have thymoma. On the other hand, some of the tumor patients have done exceedingly well. In fact, our first patient, on whom Dr. O. T. Clagett operated on Dec. 20, 1941, still has a complete remission.

Pharmacology and Anticonvulsant Spectrum of Acrolactamide (Themisone). DR. W. H. MARSHALL, ELIZABETH H. JENNEY, and DR. CARL C. PFEIFFER.

Acrolactamide (Themisone), a new anticonvulsant drug, is characterized by low toxicity in experimental animals. The oral LD_{50} in mice is 1.859 ± 0.078 gm. per kilogram. Chronic toxicity studies in mice, rats, and dogs have revealed no abnormal blood changes. Tissues removed at autopsy showed no gross or microscopic pathological changes. Pharmacologically, acrolactamide is a depressant as well as an anticonvulsant. Death is due to both respiratory and cardiac arrest. Its intravenous administration to the anesthetized dog produced no effect on the blood pressure or respiration if given at the rate of 25 mg. per kilogram per minute. Rapid

intravenous injection produced a gradual, but transient, fall in blood pressure. In a dose up to 0.9 gm. per kilogram, it had no effect on the blood pressure response to epinephrine, vagal stimulation, acetylcholine, or histamine. Concentrations as great as 50 mg. per 100 cc. were necessary to inhibit the response of the rabbit ileum to acetylcholine by 17%. Comparison of the anticonvulsant spectrum of acrolactamide with those of clinically useful anticonvulsant agents shows that, whereas acrolactamide does not receive the highest rating by all tests, nevertheless its over-all activity against a battery of tests indicates that it may be clinically effective in different types of epilepsy (Table).

Anticonvulsant Spectra of Various Drugs (Mouse) at Minimal Ataxic Doses

	Minimal Ataxic Dose (Oral) Mg./Kg.	Effectiveness Vs. Electroshock	Elevation of Experimental Convulsant Thresholds, %			
			Metrazol			
			FT*	PC*	Strychnine	Ammonium Acetate
Themisone	250	++++	55	38	25	37
Phenacemide	200	++++	28	56	7	44
Phenobarbital	37.5	+++	22	75	30	24
Diphenylhydantoin	50	++++	—	—	18	46
Trimethadione	400	±	95	91	46	10

* FT indicates first twitch; PC, persistent convulsion.

Treatment of Three Hundred Epileptic Patients with Acrolactamide. Dr. F. W. Stamps, Dr. W. H. Marshall, Dr. M. J. Orloff, Dr. F. A. Gibbs, and Dr. Carl C. Pfeiffer.

Patients resistant to other antiepileptic drugs were treated with acrolactamide (Themisone) in doses of 4 to 12 gm. a day. The control of seizures is indicated in the Table.

One hundred per cent control indicates no seizures in the past six months. The patients in the 90%-control column were those who had gone at least six months without attacks during the past two years while under acrolactamide therapy but had had a seizure within the past six months, probably due to interruption of medication. None of the disturbed patients showed accentuation of personality disorders while receiving this therapy, whereas 20% volunteered the information that they felt less nervous while under treatment. Patients with grand mal seizures

Control of Seizures with Acrolactamide

	No. of Patients	Distribution of Degrees of Control*				
		0%	50%	75%	90%	100%
Grand mal	115	17	6	31	12	49
Petit mal variant	20	8	1	3	5	3
Psychomotor	140	22	19	55	18	26
Petit mal	33	16	7	4	4	2
Jacksonian	13	3	0	3	1	6

* Expressed in number of patients.

were perhaps the most benefited, in that 52% of 115 (previously uncontrolled) were seizure-free for six months or longer. Of the 140 patients with previously uncontrolled psychomotor epilepsy, 31% were seizure-free for six months or longer. Side-effects of atrolactamide therapy and their incidence were as follows: hypersomnolence, 16 patients; leukopenia, 15; ataxia, 6; skin rash, 4; gynecomastia, 4; aplastic anemia, 3; diplopia, 1, and urticaria, 1. In five cases of leukopenia (white blood cells below 3,000 per cubic millimeter) the count returned to normal, even though the dose of acrolactamide was maintained or increased.

DISCUSSION

Dr. Richard Richter: Has Dr. Stamps subsequently withdrawn other forms of anticonvulsant medication and carried his patients for any considerable time on acrolactamide treatment alone?

DR. F. W. STAMPS: Yes. Treatment is an individual matter. When seizures are controlled, we maintain the same dose of atrolactamide and gradually withdraw the other drugs.

DR. ERNST HAASE: Although I can confirm Dr. Stamps's observation with regard to somnolence in some of the patients, others exhibited rather overactive and euphoric behavior. A senior high school student, a girl, who had been moody, crabby, depressed, and asocial, changed remarkably after she was placed under treatment with acrolactamide. She not only was free from seizures, but was cheerful and friendly and took active part in school and social affairs. Some of the patients had dilated pupils and even complained of blurred vision, suggesting an atropine-like property of the drug.

DR. F. W. STAMPS: If all other drugs are withdrawn, the sleepiness and probably some of the other side-effects are avoided. One cannot be sure that the improvement in personality and the feeling of well-being are due to acrolactamide. They may be due to withdrawal of barbiturates.

DR. F. A. GIBBS: From what we have heard, there is no doubt that acrolactamide is a very effective anticonvulsant. The results in this series of 300 cases is impressive. All who are interested in epilepsy can rejoice. Dr. Stamps pointed out, however, that this drug may produce blood damage. In one case this drug, or some other used in combination with it, produced a fatal pancytopenia. That danger is not to be forgotten. Dr. Stamps, will you tell us what measures you take to minimize this hazard?

DR. F. W. STAMPS: When one is carrying 300 patients in clinic, it is hard to make complete blood studies. We try to make a complete blood study when we start the drug, another in two weeks, and then one each month. When the patient becomes stabilized and the blood count remains constant, only a hemoglobin determination and a white cell count are done in some cases.

DR. PAUL C. BUCY: Do blood dyscrasies occur early when they do occur?

DR. F. W. STAMPS: They cannot be predicted; they occurred at the end of nine months in one case.

DR. M. A. PERLSTEIN: I have had two cases in which very good clinical results were obtained. I have not had the courage to give the large doses used by Dr. Stamps.

What happens in the electroencephalogram; is it normalized?

DR. F. W. STAMPS: We have noticed no change. I have used the drug intravenously in a few cases in which the electroencephalogram showed constant seizure activity, such as petit mal variant. We have injected 50 cc. of a 5% solution. It does not have an effect on the brain waves. The drug has another use; it is very effective in stopping status epilepticus. It does not produce the sleepiness that amobarbital and some other drugs do.

DR. PAUL C. BUCY: In line with Dr. Haase's comment, is there an atropine-like effect?

DR. F. W. STAMPS: Some one reported the case of a child with dilated pupils and urinary retention. He had difficulty in starting to urinate.

DR. PAUL C. BUCY: What about the experimental animal?

DR. W. H. MARSHALL: There was no parasympathetic blocking.

NEW YORK NEUROLOGICAL SOCIETY AND NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

Richard M. Brickner, M.D., President, New York Neurological Society, Presiding

Joint Meeting, Jan. 13, 1953

Narcophotic Stimulation of Psychiatric Patients. DR. BERNARD L. PACELLA and (by invitation) DR. JOSEPH J. DOLTOLO and DR. MURRAY S. FLEISCHER.

Narcophotic stimulation treatment was administered to a group of 89 psychiatric patients bearing various categories of diagnosis. The treatment consisted in administering about 3¾ grains (0.25 gm.) of amobarbital (Amytal) sodium intravenously, followed immediately by photic stimulation, in which the flicker frequency varied from 10 to 15 per second. The duration of application of the stimulation usually varied from three to six minutes, and the total number of treatments per patient varied from 6 to 20. No untoward reactions or complications occurred.

The treatment seemed to be helpful in certain manic patients and of some value in the less disturbed depressive patients of the manic-depressive type, particularly the recurrent, or cyclic, forms. Very little effect was noted in the psychoneurotic and schizophrenic groups.

DISCUSSION

DR. LOTHAR B. KALINOWSKY: The significance of such studies as the one presented by Dr. Pacella and his associates goes beyond the appraisal of the therapeutic value of the procedure under investigation. The idea of the French and British authors who introduced this treatment was to produce cerebral dysrhythmia. This can also be done with pentylenetetrazole (Metrazol), with nonconvulsant electrical stimuli, and, as you see now, with photic stimulation. There arise the questions whether the dysrhythmia as such is an effective therapeutic agent, and in how far some or all of those treatments which produce cerebral dysrhythmia are effective. Electrostimulation without convulsion is not considered effective in such psychotic states as those treated by Dr. Pacella with narcophotic stimulation, although it does produce dysrhythmia. If effective at all, electrostimulatory nonconvulsant treatment is so only in neurotic conditions.

DR. DAVID J. IMPASTATO: My results, using practically the same technique as Dr. Pacella's, are largely in agreement with his. Of 22 patients, 4 recovered or were much improved; 6 were improved, and 12 were unimproved. The treatment should be considered empirical, for at present it is impossible, with the little experience we have had with it, to evaluate with any degree of assurance the role, if any, the following factors may play in the curative process: photic stimulation, amobarbital sodium, the treatment situation, and the natural tendency toward recovery of the disease.

QUESTION FROM THE AUDIENCE: In the literature I do not remember that photic stimulation was done with the eyes closed. I wonder whether one should call this photic stimulation with the eyes closed.

DR. BERNARD L. PACELLA: I am in full agreement with Dr. Impastato's comment. There are many aspects of the treatment I did not go into, such as the matter of its being an office procedure, since it entails no hazards or complications, and the possibility that it can be utilized in many cases in which convulsive therapy is considered too risky.

With respect to the question concerning photic stimulation with the eyes closed or open, there are all sorts of variations in technique; many persons have used stimulation with the eyes periodically open or closed. We have given it with the eyes closed. It is to be noted that when the eyes are opened, the photic "driving" effect upon the alpha waves in the electroencephalogram may be obliterated. When the eyes are kept closed, the red part of the spectrum passes through the lids almost completely, since the eyelids act as a filter, allowing the red rays to pass; the orange-red light seems to be the most effective light for stimulation.

Blood Pressure in Small Arteries on the Surface of the Brain. DR. LESTER A. MOUNT and (by invitation) DR. ROBERT J. STROBOS and DR. JOHN J. JACOBS.

A method of taking and recording blood pressure in arteries as small as 1 mm. in diameter on the surface of the brain has been devised. This method consists of the insertion of a No. 26 hypodermic needle into the artery, with a tube connecting the needle to the Lilly capacitance manometer, and the making of a continuous blood pressure record, using a Brush recorder.

Simultaneous recordings of blood pressure were taken from the internal carotid artery in the neck and from a cortical artery during the occlusion of the carotid arteries on the ipsilateral side, on the contralateral side, or on the two sides simultaneously.

Although our series is too small to permit definite conclusions, the results suggest (1) that there is as much indication for ligation in the neck in the treatment of aneurysm peripherally located in the brain as there is in the treatment of aneurysm arising from the internal carotid artery, and (2) that one need not fear an increase in intra-arterial pressure on the contralateral side following carotid ligation in the neck.

DISCUSSION

DR. J. LAWRENCE POOL: I have seen Dr. Mount's work develop at the Neurological Institute and have seen its value proved in the treatment of aneurysms, as well as of vascular malformations of the brain, of a sort requiring ligation of the carotid artery in the neck and/or the

intracranial ligation of arterial vessels. This new application of a pressure-recording device to the blood vessels of the arteries of the brain itself is of particular value, because it provides a means of preventing hemiplegia that might follow too extensive occlusion of the carotid artery in the neck. Can Dr. Mount state what is the safe percentage of drop in blood pressure in cortical arteries?

Another point of extreme value is his demonstration that the Selverstone clamp in the neck can be almost completely tightened down, thus almost completely occluding the artery in the neck, and the pressure in the cerebral vessels will not fall to any significant degree.

I should like Dr. Mount to explain why the tubular hydraulic system is not valid in the reduction of pressures in the arteries in the brain.

Finally, there are two other points I wish to make: First, he has shown the value of these pressure recordings in obtaining information about the collateral circulations in the two hemispheres. The results of the tests on the two sides are nearly parallel in many cases he has studied, and I think they provide an answer as to why ligation is safe in one case and not in another. Second, has he correlated the pressure changes in the cortical vessels with electroencephalographic changes carried out at the same time?

Dr. M. Martin Tunis: Has Dr. Mount made any observations with this method that might clarify the following points?

1. Under the conditions of his study, how long can unilateral cervical occlusion of the carotid artery be safely maintained? With such an occlusion (either ipsilateral or contralateral), does the described drop in the intravascular pressures persist bilaterally as long as the occlusion is maintained? Is there ultimately partial recovery?

2. Is the marked decrease in pulse rate following the occlusion a reflex effect? Was the cardiac stroke volume affected analogously in any way?

With the already impaired collateral circulation, as indicated by Dr. Mount's study, a transient modest diminution of stroke volume might further diminish the blood supply to relevant areas of the cortex.

Dr. Fritz J. Cramer: Did Dr. Mount induce spasm in the cortical vessels, and how? Was the spasm general, or was it localized to the very small tree which he was testing?

Dr. Richard M. Brickner: If partial occlusion of the carotid artery causes so slight a drop in blood pressure more distally, perhaps the value of partial occlusion in the treatment of aneurysms should be reviewed. Would Dr. Mount discuss this?

Dr. Lester A. Mount: In answer to Dr. Pool's question: The safe reduction of pressure in the neck is about 70%, but the amount of reduction must be balanced with other things. We had hoped to be able to correlate it exactly, and perhaps with a sufficient number of cases we may be able to do so; but we do need to take into consideration the arteriographic findings. If an anterior cerebral artery between the internal carotid and the anterior communicating artery is not demonstrable on the arteriogram, the collateral circulation is deficient. If the opposite carotid artery cannot be filled on injection of the contrast material into one carotid artery with compression of one on the opposite side, the circulation is deficient; with our pressure readings we hope to be able to determine the amount of deficiency. Is there enough collateral circulation through the posterior communicating artery to make up for this deficiency? We have learned some things about the degree of collateral circulation, but not enough to permit the drawing of any definite conclusions. We can say that, provided the pressure is not reduced more than 50%, we are not likely to have any complications. We have not made nearly as many pressure readings from the cortical arteries as we have taken from the carotid arteries in the neck alone; so we should not be justified in making any comment on the reduction there.

In answer to Dr. Pool's question as to why the tubular hydraulic system does not apply: As you recall, in one patient there was, on bilateral compression of the carotid artery, a reduction of pressure in the cortical artery to zero, whereas in the neck it was 40/40; so there is not a solid tubular system, with which the pressure should be the same throughout.

We have not correlated the pressure and the electroencephalographic changes.

In answer to Dr. Tunis: In the patients in whom we studied the peripheral circulation simultaneously with the carotid recordings, on carotid compression there was no change in the stroke volume, in the peripheral resistance, or in the peripheral blood pressure.

In reply to Dr. Cramer's question about the method of the induction of spasm: Spasm was produced by local stimulation of the artery by the needle itself. The point of the needle stimulated the other wall of the artery. Then the artery itself, the single artery in which the needle had been inserted, went into spasm. This was not true in any of the other arteries.

In answer to Dr. Brickner: Partial occlusions as usually performed are ineffective in lowering cortical blood pressure. If pressure is recorded in the cortical artery while the Selverstone clamp is being tightened, the degree of reduction of pressure can be regulated to the desired amount.

It would seem that there is as much indication for ligation in the neck in the treatment of aneurysms peripherally located in the brain as there is for ligation in treatment of aneurysms arising from the internal carotid artery itself. We hope that with a sufficient number of cases we shall then be able to predict which patients will have complications after ligation of the carotid artery.

PHILADELPHIA NEUROLOGICAL SOCIETY AND PHILADELPHIA SOCIETY OF ANESTHESIOLOGISTS

Alexander Silverstein, M.D., *Presiding*

March 6, 1953

Use of Spinal Anesthesia. Dr. James E. Eckenhoff.

The use of spinal anesthesia is fraught with danger. Reports have indicated incidences of major neurologic sequelae to spinal anesthesia as high as 6 cases in 1,200 patients. In spite of such figures, recent data suggest that prohibitive morbidity need not be associated with the subarachnoid injection of local anesthetic drugs. A forthcoming report from the Hospital of the University of Pennsylvania will reveal the absence of a single major neurologic complication in 10,000 anesthesias with a 90% follow-up of 6 to 48 months.

The apparent answer to the problem of neurologic complications is the development of a meticulous technique of preparing equipment, performing the subarachnoid puncture, and injecting the anesthetic drug. The advantage of spinal anesthesia is its ease of administration and the excellence of surgical working conditions produced. The careful and proper use of continuous methods with injection of small doses of procaine will often enable surgical procedures to be performed on patients representing poor surgical risks or on elderly patients, with surprisingly slight disturbance to circulation, respiration, and metabolism.

Records of patients showing favorable responses to spinal anesthesia were presented. Such patients included very hypertensive patients, very obese patients, aged patients, and patients offering poor risks. Records of undesirable responses to spinal anesthesia in patients from similar categories were also shown. These records were compared with records of patients in comparable groups given general or local anesthesia who likewise reacted poorly.

The morbidity and mortality rates for spinal anesthesia need not differ from those for any other technique of anesthesia. However, the anesthetic agent or the technique of choice in any given situation is that with which the anesthetist is most familiar and can employ with the greatest facility.

DISCUSSION

Dr. Robert Groff: As you might suspect, I do not approve of spinal anesthesia. Of course, the neurologist and the neurosurgeon see the complication. My colleagues and I now have over six patients with permanent deficits. In a lad whose first opertive symptom was gradual leg weakness a mass which looked like a glioma was revealed. The spinal cord, as well as the arachnoid, was removed and the condition proved to be arachnoiditis with changes in the cord. Although their percentage is probably small, the complications, when they arise, are frequently untreatable. It seems to me that spinal anesthesia has only one thing to offer, and that is muscular relaxation. I understand that curare will produce that adequately, and therefore spinal anesthesia will not be necessary.

Dr. Michael Scott: Our experience with spinal anesthesia has been a happy one. My colleagues and I had been using spinal anesthesia for disk operations, but when the wave of

complications rose, we switched. I saw a patient from another hospital who had been given spinal anesthesia for childbirth; she had gradual development of signs and symptoms of involvement of the spinal cord, and operation revealed a neomembrane which acted like a constricting band. There was no postoperative improvement.

DR. RIGGERS: I had two cases of total paralysis following spinal anesthesia with tetracaine. In both a spinal tap was done the morning after the anesthesia, and a diagnosis of chemical arachnoiditis was made. The neurosurgeon said operation was hopeless but recommended continuous drainage of spinal fluid and intravenous administration of fluids. Over 1,600 cc. of spinal fluid was removed in eight hours. Under this regimen one patient made a complete recovery; the other has only a residual foot drop. I believe it is important to recognize the diagnosis and try to treat the complication.

DR. HELENA RIGGS: I have not seen an autopsy in any cases of this sort, but I wish to emphasize that not all complications are due to the anesthetic. I have had two cases in which other factors were responsible. In the first paralysis developed after spinal anesthesia and an intramedullary tuberculoma was found. In the second there was an epidural granuloma. These tumors were both silent clinically before the spinal anesthesia. If any disease of the spinal cord is suspected, it is best not to use spinal anesthesia.

DR. E. A. DENBO, Camden, N. J.: I saw a patient in the acute phase of poliomyelitis who was given spinal anesthesia inadvertently and, despite the acute inflammatory crisis, made a complete recovery.

DR. HENRY WYCIS: A difficulty in evaluating this procedure is the selection of sporadic cases. A cross section of the country would probably show that the incidence was low. In a series of 1,000 cases, I have had no complications. Dr. Babcock, who was the originator of this procedure, told me that of over 10,000 cases he has seen complications in only 3.

DR. R. M. SILBERSTEIN: Why is spinal anesthesia contraindicated for patients who fear it?

DR. AUSTIN LAMONT: What about the immediate mortality rate for spinal anesthesia?

DR. JAMES E. ECKENHOFF: Fear is an important contraindication, for the patient imagines all sorts of complications. The immediate mortality rate depends on the knowledge of the anesthesists as to the level of the anesthesia. I have no actual figures, but the mortality is rather low. Spinal anesthesia should be given with meticulous care. I had a case like Dr. Riggs's in which a tumor of the cord was found. The use of curare as a substitute for spinal anesthesia is still not too well accepted. The mortality rate for curare may be as high as 1 per 400 anesthesias. This does not mean that curare is a lethal drug, but it must be given with great care.

Anesthesia in Neurosurgery. DR. MARIO V. TRONCELLITI.

Anesthesia must be satisfactory to the patient and to the surgeon. To be satisfactory to the patient, it must be safe and, if possible, pleasant. This goal can be attained only by a competent anesthetist who has the means of instituting resuscitative measures immediately and who is acquainted with the physiologic changes that may occur as a result of the disease, the traumatic insult of the surgical procedure, or the anesthetic agent.

The surgeon often requires that the patient be placed in a position that interferes with normal compensatory mechanisms in a state of heavy sedation or anesthesia; for example, the prone flexed position inhibits normal respiratory excursions and may contribute to shock, owing to pressure on the inferior vena cava, with reduction in the return flow of blood. The sitting position is conductive to hypotension, since almost all the anesthetic agents cause peripheral vasodilatation.

Since the neurosurgeon must work near the orifices leading to the respiratory tract and he often chooses to employ the Bovie unit, tracheal intubation is usually mandatory, and the choice of anesthetic agents is limited to those that are nonexplosive.

Hypotensive anesthesia, whether attained by preoperative bleeding, the position of the patient, or the employment of vasodepressor drugs, has many contraindications and probably should be resorted to only in those rare instances in which bleeding would otherwise make the operation impossible.

DISCUSSION

DR. RUDOLPH JAEGER: I have never seen a complication of spinal anesthesia. Winkelman, in a series of experiments, showed that certain detergents cause complications. My associates and I began with local anesthesia and then switched to intratracheal ether anesthesia, but I agree with Dr. Troncelliti that a tube which may cause coughing is a hazard. The drug we like to use is thiopental, which can be given with the patient in any position. Hypotensive drugs are not used very extensively because there are other means. Perhaps in a case of arteriovenous aneurysm one may want hypotension. I used such a drug in one case, but it was not very effective. I have seen it used in Europe, without much benefit. As for position, I believe the patient can breathe as well on his face as on his back. I have had many in a semierect position without experiencing difficulty. One hazard of this position is air embolism.

DR. MICHAEL SCOTT: More and more, neurosurgeons are using the sitting-up position, especially for surgical lesions and tumors of the posterior fossa and cerebellopontile angle. This position is preferable, for the vision is good and gravity helps with the blood. I had an unfortunate case in which a patient with an intramedullary tumor in the cervical region stopped breathing because the flexion of the neck probably contributed to his difficulty from the high cervical tumor. I believe it is important for the surgeon and the anesthetist to be in good rapport, so that this kind of complication can be avoided.

Role of the Anesthesiologist in Diagnostic and Therapeutic Nerve Block. DR. D. DWIGHT GROVE.

Nerve-block procedures were originally devised chiefly for the production of insensitive tissues in surgery. In many instances they have been applied as diagnostic and therapeutic means.

The application of these methods has gone hand in hand with the rapid strides in contemporary medicine. Accumulated knowledge in neurologic and orthopedic surgery, of the mechanism of pain, and of the autonomic nervous system, and advances in all fields of medicine have contributed to focus attention on these procedures.

At present diagnostic and therapeutic nerve blocking procedures are utilized by many special services. Many of these procedures are relatively simple and can be performed well by the physician if he will master the method and recognize its indications and limitations.

The actual and potential value of diagnostic and therapeutic nerve block is not exhausted, and a greater application can be accomplished through an active integration of all branches of medicine.

Much discredit has come to the use of nerve blocking from the too frequent practice of "trying a block" without a reasonably accurate diagnosis. The patient's welfare is of prime importance, and the best treatment available should be offered. This may be chemical or surgical interruption of pain pathways, or it may be psychotherapeutic.

The anesthesiologist can be a part of the therapeutic team by the application of his skill in the performance of nerve blocks of merit. This should follow such consultation as is necessary to for a reasonably accurate diagnosis. The anesthesiologist can provide an important service in the instruction of physicians in diagnostic and therapeutic nerve-block procedures.

DISCUSSION

DR. AXEL K. OLSEN: I believe blocking of certain nerves is an important procedure, and the anesthetist can frequently do it better than I can. Dr. Grove stated that this technique is at the beck and call of many services. I do not think that is a very good idea. Many nerve blocks are undoubtedly done in psychoneurotic patients. Another pitfall is the use of nerve blocks to cover up a possible treatable problem. My chief quarrel with this technique is in the use of the more necrotizing agents, producing chemical and traumatic neuritis.

DR. RUDOLPH JAEGER: The only indication that I know of for alcohol-procaine nerve block is to relieve trigeminal neuralgia or to complete the destruction of a carcinoma of the cauda equina.

DR. ROBERT GROFF: It is important to caution against the use of alcohol in the subarachnoid space. I believe procaine may be of help in certain conditions. In trigeminal neuralgia it is probably the neurosurgeon's responsibility to perform the block, although I feel the anesthetist can learn to do it.

Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

Physiology and Biochemistry

ANALYSIS OF CRANIAL ARTERY PULSE WAVES IN PATIENTS WITH VASCULAR HEADACHE OF THE MIGRAINE TYPE. M. M. TUNIS, and H. G. WOLFF, Am. J. M. Sc. **224**:565 (Nov.) 1952.

Simultaneous bilateral cranial artery pulse waves were studied in subjects with vascular headaches of the migraine type. It was found that prior to the onset of the headache there was a diminished pulse amplitude, indicative of vasoconstriction and increased resistance to blood flow. After the onset of headache there were a progressive increase in pulsation amplitude and disappearance of the reflected waves in the diastolic limb. This was associated with progressive vasodilatation, hyperemia, and decreased resistance to blood flow. When there was tissue edema in the painful area, the steepness of the descending limb of the pulse wave was modified.

Slit-lamp studies of conjunctival vessels of the eye on the side of the headache indicate that the vessel walls are thickened, the intraluminal diameter reduced, and the blood flow slowed. It is inferred that the pain of vascular headache results from increased tension within or about pain-sensitive cranial artery walls. Dilatation and distention of cranial arteries are fundamental to the mechanism of the migraine type of headache.

BERLIN, Mount Vernon, N. Y.

CHANGES IN FREE AMINO ACIDS OF BRAIN AND MUSCLE AFTER TOTAL HEPATECTOMY. E. V. FLOCK, M. A. BLOCK, J. H. GRINDLAY, F. C. MANN, and J. L. BOLLMAN, J. Biol. Chem. **200**:529, 1953.

Characteristic changes appear in the brain as a result of loss of hepatic function. The concentration of free amino acids of the brain increases progressively up to approximately twice the normal value in from 13 to 24 hours after total hepatectomy in the dog. This is preponderantly due to the fivefold increase in the amount of glutamine. There is, however, no significant change in the concentration of glutamic acid. A definite, but smaller, increase in the concentration of glutamine in muscle also occurs, but this is associated with a decrease of similar degree in the concentration of glutamic acid.

PAGE, Cleveland.

METABOLISM OF CHOLESTEROL IN THE CHICK EMBRYO: I. THE SYNTHESIS OF CHOLESTEROL. W. M. STOKES, W. A. FISH, and F. C. HICKEY, J. Biol. Chem. **200**:683, 1953.

Injected carboxyl-labeled sodium acetate is continuously incorporated into the cholesterol of the fertile hen's egg during the latter half of incubation. The magnitude of incorporation averaged less than 0.5% of the injected activity over a 24-hour period. The largest percentage conversion occurred in the embryo proper at all times. However, the specific activity of the cholesterol of the membranes was always much greater than that of the embryo. Toward the close of incubation there occurs a shift of activity to the embryo from all the embryonic membranes. Two peaks of C^{14} incorporation into cholesterol are evident, one at approximately 16 hours after injection, indicating conversion from injected acetate, and the other at 168 hours, measuring the conversion from a reservoir of labeled molecules, probably fat.

PAGE, Cleveland.

STUDIES OF METABOLIC TURNOVER WITH TRITIUM AS A TRACER: II. GROSS STUDIES ON THE RAT. R. C. THOMPSON, J. Biol. Chem. **200**:731, 1953.

Tritium oxide was administered intraperitoneally to 40 rats. The animals were killed at intervals after administration, and tritium of body water and tissue-bound tritium were determined in various organ and tissue samples. The biological half-life of body water in the

rat was found to be 3.3 days. All organs and tissues sampled (except blood) contain components which lose tissue-bound tritium with a biological half-life of 80 days or longer. Evidence is presented which suggests strongly that these long-lived components represent a significant proportion of the total animal tissue.

PAGE, Cleveland.

SITES OF ORIGIN OF ELECTRIC POTENTIALS IN STRIATE CORTEX. G. H. BISHOP, and M. H. CLARE, J. Neurophysiol. **15**:201 (May) 1952.

The location with respect to depth in the optic cortex of the sources of certain components of potential in responses to single optic nerve volleys was investigated by various techniques in rabbits and cats.

The first spike is assigned to the arrival of impulses over the optic radiation; the second, to the first response of cortical cells, probably including Golgi Type II cells of Layer IV. The following two or three spikes, appearing at 1.5 msec. intervals and of 1.5 msec. durations, arise from successively higher levels of cortex.

The slow surface-positive wave underlying these spikes appears to be associated with them, the earlier part originating lower in the cortex than the later.

The negative wave immediately following the positive is found in the lower third of the cortex, probably arising from Layer VI. Since in an occasional normal record, and uniformly under the influence of strychnine, an earlier, and considerably greater, negative wave is present; and since this occupies the whole depth of the cortex under strychnine, these two negative waves are inferred to be different in origin. The late negative wave presumably arises in cells different from those responsible for the positive components. The early negative wave is assigned to conduction from the cell bodies along apical dendrites toward the cortical surface. Its absence in the normal cortical record indicates that such conduction usually does not follow upon afferent stimulation of the cortex. Strychnine, which is too weak to affect the form or intensity of the normal surface-positive components, induces the response represented by this negativity.

With very dilute strychnine, large positive responses of the cortex are followed immediately by the early negativity, but lower responses may show a delay between the positive and the early negative waves. In such cases the two negative waves can be distinguished in the same record.

The early positive wave is inferred to represent the activity of basal dendrites of the neurones, of which the spikes represent the activity of the cell bodies. The authors present a tentative description of the course of activation of cortical neurones.

ALPERS, Philadelphia.

LOCALIZATION OF ANEURIN [THIAMINE] PYROPHOSPHATASE IN THE BRAIN. D. NAIDOO, and O. E. PRATT, J. Neurol., Neurosurg. & Psychiat. **15**:164 (Aug.) 1952.

The dephosphorylation of thiamine (aneurin) pyrophosphate by brain tissue has been observed, and Westenbrink and associates described an active phosphatase hydrolyzing the phosphoric esters of thiamine. It was found that this enzyme successively removes the two phosphate groups from thiamine pyrophosphate, so that when terminal phosphate is removed, thiamine orthophosphate appears as an intermediary, which is further broken down, releasing thiamine.

The histological demonstration in brain tissue of the sites of this hydrolytic process is of interest in relation to the pathology of the nervous diseases associated with thiamine deficiency.

This paper describes and illustrates the results obtained from localizing in brain tissues the sites of enzymatic cleavage of phosphate from thiamine pyrophosphate at pH 6.9.

The sites of hydrolysis of thiamine pyrophosphate (cocarboxylase, vitamin B_1 pyrophosphate) were demonstrated in frozen dried normal rat brains. The authors point out that the histological sites at which this activity is localized and the biochemical conditions in which it can be demonstrated differ from those previously described when other phosphoric acid esters were used as substrates. The possible significance of these histological and biochemical differences is discussed.

ALPERS, Philadelphia.

MYASTHENIA GRAVIS. A. WILSON, Glasgow M. J. **33**:381 (Oct.) 1952.

Wilson discusses the problem of myasthenia gravis from the standpoint of possible causes of block at the neuromuscular junction. If deficient production of acetylcholine is at fault, this is peculiar to the motor end-plates, for it is not seen in other cholinergic nerve endings. There is no direct evidence that decreased production of the transmitter substance is present in myasthenia gravis. In stimulation of a motor nerve in myasthenia there is a decline in voltage of the action potential, as in curarization. Studies of muscle action after intra-arterial injection of acetylcholine reveal that myasthenic muscle is no more sensitive than normal muscle.

Obvious technical difficulties exist in studying cholinesterase activity at the neuromuscular junction. Moreover, it is now known that there are at least two enzymes that hydrolyze acetylcholine. It is now the consensus that there is no difference in either between normal and myasthenic serum (pseudocholinesterase) or between normal and myasthenic red blood cells (true cholinesterase). Other cholinesterase inhibitors, such as diisopropyl fluorophosphate, do not produce relief of symptoms after injection, such as is seen with neostigmine. However, if the administration of diisopropyl fluorophosphate is continued for over two weeks, some increase in muscle strength is observed. If neostigmine is added, there is enhancing of this effect, even without further change in the cholinesterase activity of the blood.

Wilson has repeated Walker's demonstration of the evidence for a circulating substance, wherein exercise of one limb increases the other myasthenic symptoms, which effect is blocked by occluding the venous return of the exercised extremity. Serum from myasthenic patients after exercise blocks the neuromuscular junction in the frog nerve-muscle preparation; this effect is absent if the patient is taking neostigmine.

The author has extracted, with acetone, the thymus glands of patients with myasthenia who have been subjected to thymectomy. This extract has shown evidence of blocking of the neuromuscular junction in biologic preparations, and the greatest effect was seen in the extracts of glands from patients who obtained the most beneficial results from thymectomy.

SIEKERT, Rochester, Minn.

Neuropathology

PROBLEM OF MUSCULAR DYSTROPHIES. R. H. RAMSEY and H. R. MCCARROLL, J. A. M. A. **150**:659 (Oct. 18) 1952.

Ramsey and McCarroll analyze a series of 255 cases presenting characteristics of progressive degenerative disease of muscles or motor nerves. Of this series, 231 are classified as cases of primary myopathy or progressive muscular dystrophy, 227 being of the childhod type and 4 of the facioscapulohumeral type.

The childhood type of progressive muscular dystrophy is a heredofamilial disease that, in this series, appeared as early as one year and as late as 13 years of age. Males were involved eight times as frequently as females. The clinical features of the disease are outlined. There is no known effective treatment. Creatine and creatinine excretion studies were carried out on a few patients only, and the results routinely conformed to the reported findings of an increased excretion of creatine and a decreased excretion of creatinine. It is pointed out that elective surgical treatment of these patients should be avoided. Muscle biopsies on six patients of this group showed normal nerve and vascular elements, with various stages of muscle-fiber degeneration. Of the total group of 227 patients, 110 were followed for periods up to 27 years, 64 had died, the average age of death being 16 years. Of the 46 still living, 42 were complete invalids.

Only four patients had the facioscapulohumeral type. This disease usually appears at an older age, precluding its frequency in a children's clinic. The alteration in creatine and creatinine excretion and the micropathological conditions are identical in the two types, adding support to the concept that the underlying defect is the same in the two diseases. However, in the facioscapulohumeral type the initial symptoms usually appear in adolescence, and the prognosis is much better, as many of the patients are not seriously disabled until late in life.

In this series 24 cases were classified as instances of primary neuropathies, 20 being of the Charcot-Marie-Tooth type of muscular atrophy and four of the Werdnig-Hoffmann type. In

the first type, the onset may be from the first year to middle life, and the speed of progression varies from total disability in a few years to absence of serious disability for several decades. No known treatment affects the cause of the disease process, but corrective surgery of foot deformities may reduce the disability appreciably. The muscle atrophies are due to loss of innervation. Muscle biopsies done in three cases revealed characteristic changes, that is, a grouping of bundles of atrophic fibers adjacent to bundles of normal fibers, suggesting that an involved motor nerve may exist adjacent to a normal motor nerve and produce a patchy atrophy.

Patchy atrophy is also characteristic of the muscles in the Werdnig-Hoffmann type of progressive muscular atrophy. This disease is usually fatal in the first few years of life, and autopsy shows atrophy and loss of the large motor cells of the anterior horns of the spinal cord, in addition to the patchy muscular atrophy.

ALPERS, Philadelphia.

Psychiatry and Psychopathology

CROSSED LATERALITY IN CHILDREN: REPORT OF PEDIATRIC, PSYCHIATRIC, AND PSYCHOLOGICAL ASPECTS OF THREE CASES. M. SELDOWITZ and A. B. BERMAN, A. M. A. Am. J. Dis. Child. **85**:20 (Jan.) 1953.

The authors report three cases of children, aged 6⅝, 7, and 7 years, respectively, with crossed or mixed laterality and the results of psychometric examinations. In this condition the preferred handedness is opposite the side of the dominant eye. Though the intelligence quotients were normal or superior, each child showed marked learning difficulties and inattentiveness. All presented severe emotional difficulties, disturbances of personality, and problems of behavior and had emotionally disturbed parents and home environments. On the vocabulary subtest of the Terman-Merrill Revision the patients showed they were at least one year ahead of their chronologic ages. On the subtest for 7 years all failed in copying the figure of a diamond; their figures were small and irregular. The Wide Range Achievement test revealed that they were deficient, and confusional trends, reversals, and mirror writing were noted. Their reproductions of the Bender Gestalt Patterns revealed significant signs of disturbance in the visual-motor integration. The "Draw-A-Man" test revealed inadequate perception of the human in space, some organic concomitants, and regression.

SIEKERT, Rochester, Minn.

ELEVATED SERUM POTASSIUM AS A POSSIBLE CAUSE OF DEATH IN HYPERACTIVE STATES. N. ENDE, F. G. BRAZDA, and J. ZISKIND, Am. J. M. Sc. **224**:638 (Dec.) 1952.

A man aged 33 with delirium tremens died after one hour of extreme sustained hyperactivity. It was found that his serum potassium level was 12 mEq. A blood potassium level of 10 mEq. is considered lethal. It was found in normal males that running was followed by elevated blood potassium levels. Patients who had grand mal seizures for 30 to 45 secenods had a rise of 1 to 1.5 mEq. of blood potassium. It is suggested that the immediate cause of death in states of hyperactivity may be hyperkaliemia.

BERLIN, Mount Vernon, N. Y.

Meninges and Blood Vessels

ALCALIGENES FAECALIS MENINGITIS COMPLICATED BY HYDROCEPHALUS IN A PREMATURE TWIN: REPORT OF CASE; INTRAMUSCULAR CHLORAMPHENICOL THERAPY. ROBERT O. WARTHEN, A. M. A. Am. J. Dis. Child. **84**:729 (Dec.) 1952.

Warthen reports the third premature infant to recover from meningitis—the first premature infant with Alcaligenes faecalis meningitis and the ninth with this organism.

A girl, weighing 1,930 gm. at birth, progressed satisfactorily until the age of 9 days, when the temperature rose to 100.2 F. Examination revealed nothing abnormal except for a flat, somewhat tense anterior fontanelle. The spinal fluid was xanthochromic; the reaction for globulin was 4 +, and the total protein was 690 mg. per 100 cc. The cell count was 800 red cells and 450 leucocytes per cubic millimeter, with 70% neutrophiles and 30% lymphocytes. The smear showed many Gram-negative bacilli; the culture yielded a faecalis. Chloramphenicol was

given, 250 mg. intramuscularly twice a day. The temperature was then 102 F., and four hours later frequent intermittent clonic convulsions appeared. Eight hours after antibiotic therapy the temperature was normal.

Spinal puncture after one week of treatment yielded only a small amount of a yellow fluid, most of which soon coagulated. The culture and smear showed no pathogens. The circumference of the head was 30.8 cm. Eight days later the fontanelles were full and tense, and the head circumference was 33 cm. Bilateral subarachnoid taps revealed no excessive fluid. Lumbar spinal fluid contained 1,760 mg. of protein per 100 cc. Antibiotic therapy was discontinued after 17 days of treatment. At 6 months of age the head circumference was 59 cm., and the patient suddenly died.

Examination revealed bronchopneumonia. All cranial sutures were separated widely. The brain weighed 3,005 gm. The cerebral tissue was markedly thinned, and the ventricular system was dilated, containing approximately 1,500 cc. of yellow fluid. The basilar meninges were thickened and the subarachnoid space obliterated. There were marked cellular degeneration and subpial fibrosis.

SIEKERT, Rochester, Minn.

COCCIDIOIDAL MENINGITIS OF LONG DURATION: REPORT OF A CASE OF FOUR YEARS AND EIGHT MONTHS' DURATION, WITH NECROPSY FINDINGS. E. ROSEN and J. P. BELBER, Ann. Int. Med. **34**:796 (March) 1951.

A case report of coccidioidal meningitis of four years eight months' duration is presented, with clinical and necropsy findings. This is the longest reported duration for this disease. The correct diagnosis was not established until the fifth year of illness, despite extensive study during six previous periods of hospitalization in four different hospitals.

The antemortem diagnosis of coccidioidal meningitis is not difficult if the disease is considered and appropriate studies are performed. The history may be of inestimable value if presence in an endemic area can be established. The occurrence of respiratory symptoms or erythema nodosum shortly thereafter is particularly suggestive, although the primary infection may have been subclinical. The course is subject to considerable variation but is usually protracted, subject in some instances to remissions and exacerbations. Symptoms and physical signs are not characteristic and depend upon the localization of lesions. Headache, nuchal rigidity, stupor, weakness, and mental changes may be encountered, as well as evidence of more localized involvement of the central nervous system.

Spinal fluid examinations usually reveal characteristic abnormalities which strongly suggest the possibility of coccidioidal meningitis, namely, a colloidal gold curve of dementia paralytica type, marked elevation of spinal fluid protein, low sugar content, and a variable cell count, with a majority of lymphocytes and frequently a high number of eosinophiles in proportion to the polymorphonuclear cells present. Isolation of the organism from the spinal fluid by animal inoculation or cultures would be conclusive, but the organism is frequently difficult to recover; so a negative result does not exclude the disease. Serologic studies approach a high degree of specificity. Blood complement fixation and precipitin tests in significant titers definitely indicate activity. The authors stress the fact that a conclusive diagnosis of coccidioidal meningitis can be made on the basis of significant amounts of complement-fixing antibody in the spinal fluid. The value of this test is not limited to diagnosis, as serial determinations are helpful in judging prognosis.

When the diagnosis was finally established in this case, it was at once evident that this patient's illness was in every way classic for a primary coccidioidal pulmonary infection followed by early dissemination to the meninges and chronic meningitis of long duration. The diagnosis was established by serologic tests, and a positive spinal fluid culture was obtained on one occasion.

The striking features of the necropsy included an extensive basilar meningitis, ependymitis, and evidence of previous primary coccidioidal infection in the hilar lymph nodes.

ALPERS, Philadelphia.

FACTORS INFLUENCING THE DEVELOPMENT OF CEREBRAL VASCULAR ACCIDENTS: I. ROLE OF CARDIOCIRCULATORY INSUFFICIENCY. G. WILSON, C. RUPP, JR., H. L. RIGGS, and W. W. WILSON, J. A. M. A. **145**:1227 (April 21) 1951.

The renaissance of interest in the therapy of cerebral vascular lesions suggested that a more detailed study of the general cardiocirculatory status of patients with stroke might disclose further clues helpful in the comprehension of the pathophysiologic mechanism and in the establishment of a more rational therapeutic approach.

In a series of 542 cases in which an acute cerebral vascular accident was demonstrated at necropsy, the past medical history, clinical examination, or autopsy revealed evidence of cardiocirculatory insufficiency in 451 (85%). These studies were not concerned with whether cerebral vasospasm does or does not exist. The available evidence points away from the existence of any appreciable neurovascular factor. In the presence of generalized circulatory inadequacy, however, the concomitant cerebral anoxia might well account for the local vascular changes concerned with the production of a cerebral vascular lesion.

The authors believe preventive measures and therapy should be directed toward maintaining the general circulatory status at a maximum level in order to eliminate one of the causative factors in cerebral vascular accidents.

ALPERS, Philadelphia.

CEREBRAL ANGIOGRAPHY. A. UIHLEIN, Proc. Staff Meet., Mayo Clin. **26**:133 (April) 1951.

The percutaneous, or closed, technique of cerebral angiography, similar to that described by Poppen and his co-workers, is the method employed at the Mayo Clinic. One hundred cerebral angiograms, made on 77 patients, are here reported. The dye was injected into the common carotid artery. In 31 patients suspected of having a brain tumor, 16 lesions were identified by cerebral angiography (52%). In 17 of 36 patients suspected of having a subarachnoid hemorrhage a vascular lesion was demonstrated by angiography (47%). In six patients the angiograms did not indicate a brain tumor, the presence of which was later verified. For two patients the angiograms were interpreted as indicating a brain tumor, but the diagnosis could not be verified at operation. Unsatisfactory angiograms were obtained on 10% of patients, owing to technical difficulties.

Uihlein presents some of the complications of angiography. He describes an inexpensive but very satisfactory rapid roentgen casette changer built at the Clinic. From these studies he concludes that cerebral angiography is a safe and helpful diagnostic aid in the localization of intracranial lesions.

ALPERS, Philadelphia.

Diseases of the Brain

VIRUS ENCEPHALITIS DURING A POLIOMYELITIS EPIDEMIC: A REPORT OF FIVE CASES. I. DRAVIN, J. H. COFFEY, W. C. DINE, Ann. Int. Med. **34**:705 (March) 1951.

Five patients with virus encephalitis were admitted within a six-week period during a moderately severe epidemic of poliomyelitis. In four of these the disease was identified as western equine encephalitis, and in one as St. Louis encephalitis, by complement fixation and neutralizing studies.

The clinical pictures of western equine and St. Louis encephalitis are indistinguishable. The definitive diagnosis depends upon the neutralization and complement fixation tests. The cases presented here illustrate the extreme variability in the severity of western equine encephalitis, from the mild infection seen in one case to the extremely severe, fulminating form, seen in two cases.

All the patients recovered with only symptomatic, nonspecific therapy, despite the extreme severity of the disease in two. The newer antibiotics, aureomycin and chloramphenicol, were unavailable, but they should be tried in cases of virus encephalitis, since certain other virus diseases have responded to them.

During the period in which these cases occurred, 18 cases of poliomyelitis were reported. Because of a similar seasonal incidence, as well as the occurrence of many of the same clinical

features in the two diseases, it is probable that many cases of virus encephalitis have been erroneously diagnosed as poliomyelitis. A spastic type of paralysis favors the diagnosis of encephalitis, but in nonparalytic forms serologic studies may be necessary for differentiation.

ALPERS, Philadelphia.

CEREBRAL LESIONS IN CONGENITAL HEART DISEASE. M. BERTHRONG and D. C. SABISTON, JR., Bull. Johns Hopkins Hosp. **89**:384 (Nov.) 1951.

Berthrong and Sabiston reviewed the autopsy findings in 162 cases of serious congenital heart disease, 135 of the cyanotic and 27 of the acyanotic type, with special regard to the occurrence of all types of cerebral lesions, and attempted to determine, if possible, the pathogenesis of such lesions.

They found that cerebral lesions of different types occur with greatly increased frequency in patients with congenital heart disease. In patients with cyanotic heart disease, including those who have had surgical procedures, cerebral infarctions are particularly common, occurring in 25 of the 135 cases. Cerebral necroses, as a result of the greatly impaired tissue oxygenation without vascular occlusions, may account for a relatively small number of cases of microscopic lesions. The majority of the infarcts are the result of vascular occlusions.

The authors emphasize the important role of polycythemia in the production of intravascular thromboses as a cause of infarcts and discuss the close similarity in this respect of these cases to cases of polycythemia vera in adults.

Both arterial and venous cerebral thromboses occur. It is not known whether the thromboses leading to the arterial occlusions usually develop in peripheral veins, to reach the cerebral arteries as paradoxical emboli through cardiac defects, or form in the cardiac chambers to embolize the brain, or develop in situ in the cerebral arteries; but all mechanisms may occur. Venous thrombi which are seen or are inferred to exist from hemorrhagic infarctions are more common than arterial occlusions.

The severe surgical procedure necessary for the alleviation of these cardiac malformations imposes the additional factors of shock and hemoconcentration on the already increased tendency to thrombosis. Hemorrhagic infarctions are particularly frequent in the immediate postoperative period. The authors note the part played by the common attacks of increased cyanosis and fainting in increasing the tendency to thrombosis by further reducing the rate of cerebral blood flow.

Brain abscesses also occur with increased frequency in patients with cyanotic heart disease.

Patients with acyanotic heart disease also present many cerebral lesions, but these are often of a nonthrombotic origin or, when they are due to thrombosis, causes for such thromboses are obvious. A very high incidence of congenital aneurysms of the circle of Willis in patients with coarctation of the aorta is reported.

ALPERS, Philadelphia.

STATUS EPILEPTICUS COINCIDENT WITH USE OF PITUITARY ADRENOCORTICOTROPIC HORMONE [CORTICOTROPIN]: REPORT OF THREE CASES. A. DORFMAN, N. S. APTER, K. SMULL, D. M. BERGENSTAL, and R. B. RICHTER, J. A. M. A. **146**:25 (May 5) 1951.

While investigating the therapeutic effects of corticotropin (ACTH) on connective tissue disease in children, Dorfman and his co-workers observed in 3 of the 40 patients episodes of status epilepticus lasting from five to seven hours. In these instances the spinal fluid protein was temporarily elevated, and abnormal bursts of electrical activity, as well as neurologic signs, persisted long after the restoration of consciousness. The first of these patients, under observation for more than one year at the time of report, had widespread brain damage. Abnormal neurologic signs were present in the second patient three weeks after the convulsive episode, but mild personality changes were the only residuals. The third patient had no apparent neurologic damage at the time of writing. The cases are described in detail, and the authors point to convulsive episodes as another possible danger in the use of corticotropin and cortisone.

ALPERS, Philadelphia.

RHYTHMIC PALATOPHARYNGEAL MYOCLONUS. MORTON M. STERN, J. Nerv. & Ment. Dis. **1**:48 (Jan.) 1949.

Stern reviews the syndrome of rhythmic palatopharyngeal myoclonus and reports a case in which it was associated with severe closed head trauma. The patient had been unconscious for several hours; on the 21st day he noticed constant clicking noises, especially in his left ear. Examination of the pharynx revealed rhythmic, synchronous bilateral myoclonic movements of the soft palate, uvula, pharynx, and base of the tongue, at a rate of 120 to 140 per minute. When the mouth was open, there were periods of 5 to 10 seconds in which the movements were barely perceptible; swallowing and coughing decreased this latent period. The movements were synchronous with the clicking noises, and the latter persisted during sleep. Pressure on the eyeballs or the carotid arteries caused a momentary increase in the rate. Fluoroscopic examinations revealed no myoclonic movements of the diaphragm, lungs, stomach, or esophagus. Over a period of four years there has been no response to any medication or change in the clicking noises, but the palatal myclonus is harder to elicit.

The author believes that the syndrome in this case could be due to thrombosis of a small branch of the left vertebral artery affecting the olivodentate-tegmental tract complex.

The author compares the syndrome to the rhythmic reciprocating expansion and contraction of the oral cavity with corresponding relative negative and positive pressures, such as in gill-breathing fishes. He points out (1) that the evolution of lungs in the higher vertebrates dispensed with the branchial structure's function of water breathing and that in humans the first branchial arch and the first branchial pouch furnish the very structures that are involved in rhythmic palatal myoclonus, and (2) that the olivodentate complex is poorly differentiated in fishes but maximally developed in man. Thus, the author considers rhythmic palatopharyngeal myclonus as an accessory respiratory reflex that becomes active when its regulators are damaged.

FARMER, Philadelphia.

SUBDURAL EFFUSIONS IN INFANCY: TWENTY-FOUR CASES. A. N. GUTHKELCH, Brit. M. J. **1**:233 (Jan. 31) 1953.

Guthkelch presents a study of 24 cases of subdural effusion in infancy; 18 cases were of subdural hematoma, 5 of complicated purulent meningitis, and 1 of thrombosis of the sagittal sinus. The commonest symptoms in cases of subdural hematoma, in their order of frequency, were convulsions, vomiting, and irritability. Guthkelch considers subdural tap the only diagnostic procedure of value. Treatment consists in daily subdural taps for 10 to 14 days, after which craniotomy may be performed. Guthkelch also performed subdural taps once or twice in the first postoperative week. Of 16 infants treated in this way, Guthkelch has reason to believe that 10, or possibly 11, "will grow up into normal children."

It is generally agreed that subdural effusions should be suspected in any infant with meningitis whose clinical progress is unsatisfactory after three days of treatment or in whom fever, vomiting, convulsions, or a tense fontanel persists. Guthketch believes that with early diagnosis the results of treatment should approach those obtained in infantile subdural hematoma.

A case of subdural effusion complicating sagittal-sinus thrombosis is also presented. On the basis of this case, as well as a study of others, Guthkelch concludes that "cerebral thrombophlebitis, whether it occurs from extension of infection from purulent meningitis or from a focus elsewhere, may give rise to a subdural effusion, and that the likely mechanism is the giving way of the necrotic walls of veins crossing the subdural space."

ECHOLS, New Orleans.

Peripheral and Cranial Nerves

RESULTS OF A SYSTEMATIC INVESTIGATION OF THE CAUSES FOR A TEMPORARY INCREASE IN THE NEUROLOGIC COMPLICATIONS OF DIPHTHERIA. W. SCHEID, and H. WIECK, Schweiz. Arch. Neurol. u. Psychiat. **69**:269, 1952.

In Germany, as well as in other countries, there was a noteworthy increase in the neurologic complications of diphtheria during the later years of World War II and the years immediately following. The authors' material consisted of 2,292 cases of faucial diphtheria observed from

both the general clinical and the neurologic standpoint from 1946 to 1949. The respective percentages of neurologic complications for 1946 and 1947 were 25.5 and 27.3. Thereafter the percentage fell rapidly, reaching 4.2 in 1949. Neurologic complications developed in 76% of severe cases of diphtheria and in only 2% of the mild cases. A series of 1,110 cases coming under observation 4 days or less after onset of diphtheria and followed longer than 60 days were selected for more exhaustive study. In this group the frequency of neurologic complications likewise stood in direct proportion to the severity of the initial infection. In all the mild cases of diphtheria muscular weakness was limited to the throat. The extremities, on the other hand, became involved in only the severe and the moderately severe cases. In all but 3 of the 35 cases of severe polyneuritis there was a history of diphtheria of the severe type. These results tended to refute an older view that polyneuritis frequently develops after diphtheria of mild degree. Decreasing mortality rates corresponded with the progressive decline in the frequency of neurologic complications.

Results of clinical study and epidemiologic data indicated that neurologic sequelae had diminished in number because the morbidity rate of diphtheria had likewise fallen and cases of very severe faucial diphtheria had become rare. The authors found nothing to support the assumption that decreasing frequency of neurologic complications was due to improved living conditions. On the contrary, their results indicated that the diphtheritic toxin itself played the decisive role in the pathogenesis of neurologic complications.

DANIELS, Denver.

Vegetative and Endocrine Systems

SERUM NEURITIS. I. FISCHER, Ann. Int. Med. **35**:922 (Oct.) 1951.

Serum sickness has been estimated to follow the injection of various sera in about 15% of all cases in which they are used. As a rule, serum sickness is a transient affection, which responds promptly to the proper treatment (chiefly epinephrine) and which terminates in complete recovery. Occasionally, however, it is followed by so-called serum neuritis.

Fischer reviews certain important features of serum neuritis, as they are emphasized in the literature. In the majority of the reported cases the disorder followed the injection of tetanus antitoxin. Involvement of the peripheral nerves is the most frequent manifestation. Neuritic symptoms as a rule occur when serum sickness is most intense, although they may appear almost immediately after the onset or when the attack has almost disappeared. The course of events is usually that of severe pain in the neck, shoulders, arms, or legs, followed within hours or days by flaccid paralysis, muscle tenderness, and muscle atrophy. Loss of weight is frequently extreme. The pain may disappear promptly or may last for days, or even months. It is characterized by extreme severity. About 20% of all patients, according to Thompson and Tombleson, are left with permanent residua in the affected extremity, but the majority recover completely with such measures as general nutritive and vitamin therapy, immobilization of the affected part, local application of heat, and, later, physical therapy with graduated exercises.

In most respects, the case Fischer reports here fits into the pattern of other recorded cases, except that the condition occurred in a patient with a strongly psychotic background. Serum sickness developed on the eighth day after a prophylactic injection of tetanus antitoxin and was, as usual, transient. Serum neuritis developed 48 hours later. All manifestations had completely disappeared when the patient was hospitalized except for the local neuritic complication. The serum neuritis affected the brachial plexus, as it oftenest does, and the history of the intractability of the pain, in spite of ample sedation and analgesic medication, was entirely typical.

The patient remained in the hospital for 14 days. The brachial neuritis showed some improvement under immobilization, general supportive and vitamin therapy, and the local application of heat. Her mental and emotional status, however, deteriorated. She was on admission, and continued to be, in a highly emotional state, with frequent outbursts of crying, complaints of personal problems, etc. She was removed to another institution, where she remained for eight months.

She was reexamined 10 months after the onset of the serum neuritis. At this time abduction of the right arm was possible, but the muscles of the right shoulder and upper arm showed

marked atrophy, and there was considerable difference in the strength of the hand grip on the right and on the left side. The muscles of the neck were stiff and were weaker than on first examination. There had been moderate loss of weight. The patient seemed somewhat more stable emotionally as the result of the intensive psychiatric therapy she had received during the eight-month period of hospitalization.

Fischer points out that this patient's strongly psychotic background probably had nothing to do with the development of the serum neuritis, but the serum sickness and subsequent neuritis undoubtedly precipitated the psychotic episode, for which a long period of treatment was necessary. He calls particular attention to the possible medicolegal aspects of the condition.

ALPERS, Philadelphia.

Treatment, Neurosurgery

HYDRANENCEPHALY. J. T. OLIVE and JAMES W. DUSHANE, A. M. A. Am. J. Dis. Child. **85**:43 (Jan.) 1953.

Hydranencephaly, a congenital anomaly, consists of absence of the cerebral hemispheres, together with intact meninges and skull. Early the skull is normal in size, and in the first few weeks the reactions are normal. Retardation of neuromuscular development and enlargement of the head are not seen until the infant is several months of age.

A girl, 4 weeks of age, had failed to gain and was restless. She was born at term after an uncomplicated pregnancy. She cried and breathed spontaneously; no cyanosis was observed. A high-pitched, "whining" cry was noted soon after birth. In about three weeks some enlargement of the head was seen and there was no response to bright light. Examination disclosed a normal-appearing baby. Movements were normal. She sucked vigorously and responded to noise but not to light. Tendon reflexes were active, and the Moro reflex was present. Ocular movements were dissociated. The cranial sutures were separated and seemed to be floating. A tympanic note was present when the skull was percussed. Transillumination of the head disclosed diffusion of light. Vascular shadows of the scalp were clearly visible. The electroencephalogram revealed no evidence of electrical activity. The patient died at the age of 7 months.

The authors stress the importance of early diagnosis and the difficulties of diagnosis early in life. Transillumination of the head is the most valuable aid.

SIEKERT, Rochester, Minn.

NEW TREATMENT FOR HEREDITARY (HUNTINGTON) CHOREA. D. GOLDMAN, Am. J. M. Sc. **224**:573 (NOV.) 1952.

Six patients with Huntington's chorea were treated with procaine amide hydrochloride. Treatment was begun with 0.25 gm. four times a day and gradually increased over a two- to four-week period until 1.0 gm. four to five times a day was being administered. All patients had mild to marked reductions in the severity of the chorea, but there was no improvement of the patients' mental status. The side-reactions of the treatment consisted of faintness, somnolence, paresthesia in the extremities, and dryness of the mouth. Patients with paralysis agitans and myoclonic tics were not benefited.

BERLIN, Mount Vernon, N. Y.

TREATMENT OF POST-PNEUMOENCEPHALOGRAPHIC HEADACHE WITH β-PYRIDIL CARBINOL TARTRATE (RONIACOL TARTRATE). R. M. N. CROSBY, Am. J. M. Sc. **225**:61 (Jan.) 1953.

Roniacol (β-pyridil carbinol tartrate), a vasodilating drug analogous to nicotinic acid, was administered every three hours in doses of 75 to 125 mg. following pneumoencephalography. A control group given codeine and acetylsalicylic acid after "total replacement" air encephalography, had headache for an average of 4.3 days, but a group given similar medication and roniacol had headache for an average of 1.8 days. There was no effect on blood pressure. Flushing and dizziness were the only significant side-reactions.

BERLIN, Mount Vernon, N. Y.

SELECTIVE USE OF ELECTROCONVULSIVE THERAPY IN MANIC PATIENTS. BURTRUM C. SCHIELE and ROBERT A. SCHNEIDER, Dis. Nervous System **10**:291-297 (Oct.) 1949.

The value of electroshock in the treatment of manic patients has not been clearly established, and a brief review of the pertinent literature makes it evident that there is no unanimity of opinion as to the efficacy of the therapy in cases of this reaction. Some investigators believe that the electroconvulsion is as effective in manic states as in depressions; an opposing school states that results are far inferior. From their service at the University of Minnesota the authors report 29 cases and describe 3 in detail. They conclude that a quieting effect is noted, which may be life-saving in delirious mania, that the length of hospitalization is shortened, and that the patient becomes more accessible to psychotherapy. It is estimated that electroshock is 75% as effective in manic as in depressed patients. Favorable prognostic factors are an illness of short duration and acute onset, a well-integrated prepsychotic personality, and predominantly exogenous precipitating causes. Unfavorable factors include the circular type of the disease, an admixture of schizoid or psychopathic traits, and prior unsuccessful electroconvulsive therapy. The manic patient requires a greater number of treatments at more frequent intervals than the depressed patient, and he tends to relapse more readily.

BEATON, Tucson, Ariz.

ELECTROSHOCK THERAPY IN NEURODERMATITIS. W. CRADDOCK and G. C. KREBS, Dis. Nervous System **10**:331-333 (Nov.) 1949.

A case is described of electroconvulsive treatment of a neurotic patient with severe neurodermatitis. This is believed to be unique in the literature, though there have been reports of improvement in skin lesions in psychotic patients undergoing such therapy. A white man aged 24 had neurodermatitis in 1943. He was treated dermatologically in 1946, and in 1947 he was given a course of subshock insulin therapy, with betterment of the skin condition. This treatment was discontinued because of "adverse reactions." Later that year a remission occurred after intensive dermatologic attention and the institution of an elimination diet. However, there were recurrent exacerbations, and in early 1948 he was subjected to six grand mal electroshocks, with marked decline in the eruption. That summer he again became very ill and was administered a series of 13 electroconvulsions. His neurodermatitis promptly and completely subsided and has remained in abeyance ever since. The authors feel that the prognosis is guarded but state that electroshock gave more beneficial results than any other therapy attempted for this patient.

BEATON, Tucson, Ariz.

TRANSORBITAL LOBOTOMY: SURVEY AFTER FROM ONE TO THREE YEARS. WALTER FREEMAN, Dis. Nervous System **10**:360-363 (Dec.) 1949.

This is a report on 98 patients who have undergone transorbital lobotomy between 1946 and 1948. Among the advantages of the procedure, as compared with major leucotomy techniques, are speed, simplicity, the absence of untoward personality changes, and safety. In this series there were no surgical deaths, only one serious hemorrhage, and two instances of transient hemiplegia. The operation is widely applicable, since it lends itself to performance by the psychiatrist without facilities for neurosurgery. The main disadvantage of transorbital lobotomy is its limited effectiveness. It fails oftener than major leucotomy in the chronically disturbed schizophrenic patient, in the patient with long-standing pain, and in the patient with intractable involutional depression. Objections based on the dangers of a "blind" procedure and on the possibility of abuse of a simple procedure are felt by Freeman to be unimportant. Considering the fact that most of the cases made available for transoribital lobotomy are those of deteriorated institutional patients, the results are satisfactory. Of 98 patients, the status of 62% was "fair" or "good," and 50% have been able to return home.

BEATON, Tucson, Ariz.

TREATMENT OF HICCUPS. A. F. GIGOT and P. D. FLYNN, J. A. M. A. **150**:760 (Oct. 25) 1952.

Benign, self-limited hiccup is a common phenomenon. However, persistent hiccup may cause the victim great distress and be refractory to most treatments.

The etiology of hiccup is complex. There are many peripheral and central causes. In treatment the cause should be corrected whenever one is suspected. Even though the cause remains

unknown, several drugs and procedures may be used as a rational treatment for intractable hiccup. The authors stress the importance of following a definite sequence of therapeutic steps until the condition is relieved and give the following outline:

1. Counterirritation. Many patients respond to digital compression of the eyeballs, maintained for several minutes, or vomiting, initiated by pharyngeal irritation or apomorphine.

2. Gastric lavage. If counterirritation fails, the stomach should be washed out to remove any irritants.

3. Atropine. This drug, given intravenously in high doses, $\frac{1}{150}$ to $\frac{1}{50}$ grain (0.4 to 1.20 mg.), acts by blocking the vagal limits of the reflex arc.

4. Heavy sedation.

5. Carbon dioxide, by inhalation. High concentrations of carbon dioxide in air and blood from the lung produce a considerable increase in the depth of respiration.

6. Phrenic nerve block. This can be accomplished by blocking or crushing one or both phrenic nerves, and so interrupting the efferent limbs of the reflex arc.

Gigot and Flynn outline both preventive and remedial measures for the treatment of hiccup during surgical procedures, and they again stress the importance of following a definite sequence of therapeutic measures until permanent relief is obtained. ALPERS, Philadelphia.

EFFECTS OF INTRACAROTID ADMINISTRATION OF NITROGEN MUSTARD ON NORMAL BRAIN AND BRAIN TUMORS. J. D. FRENCH, P. M. WEST, F. K. VON AMERONGEN, and H. W. MAGOUN, J. Neurosurg. **9**:378 (July) 1952.

The relative effectiveness of intravenous administraton of nitrogen mustard (methyl-*bis* or *tris*-[β-chloroethyl]-amine hydrochloride) in the palliative treatment of neoplastic diseases has been reported since 1942. Recently Bierman and Klopp and their associates have devised techniques for the administration of nitrogen mustard in high dosage directly to a tumor by way of its arterial blood supply and have found even radioresistant neoplasms to be responsive under these conditions, particularly those of the liver.

The possibility of treating intracranial malignant growths was suggested by reports of such regional therapy, since it was felt that the high resistance of nerve tissue to radiation might permit administration of a radiomimetic drug in sufficient dose to damage the neoplasm without destroying normal brain. For this reason, experiments were performed on cats and monkeys to study the effect on the function and structure of the brain produced by the injection of nitrogen mustard (methyl-*bis* [β-chloroethyl]-amine hydrochloride) into the carotid artery. These effects were correlated with those observed after similar injections in three patients with primary or metastatic cerebral disease.

French and his co-workers conclude that nitrogen mustard is too toxic to normal endothelium and brain tissue to make its use in this capacity possible. Limiting factors, no matter what the dose or frequency of injection, seem to be not only the obvious toxicity of the substance to normal brain tissue but also the apparent impossibility of controlling its dispersion into the diseased area alone. In animals and patients alike toxic effects were either diffuse, involving frequently both hemispheres, or patchy, indicating that any part of the intracranial vascular distribution could receive the bulk of the injected substance when instilled in an area as remotely situated as the main trunk of the vessel in the neck. Selective absorption of HN_2 into an area containing a neoplasm by virtue of a local alteration in the blood-brain barrier appears impossible, owing to the severe endothelial toxicity of the substance. ALPERS, Philadelphia.

News and Comment

AMERICAN PSYCHOSOMATIC SOCIETY

At the annual business meeting of the American Psychosomatic Society, held on April 18, 1953, the following persons took office: George L. Engel, M.D., president; Lawrence S. Kubie, M.D., president-elect; Theodore Lidz, M.D., secretary-treasurer. Elected to council positions were Robert A. Cleghorn, M.D.; Jacob E. Finesinger, M.D., and Jurgen Ruesch, M.D.

NORTH PACIFIC SOCIETY OF NEUROLOGY AND PSYCHIATRY

At the annual meeting of the North Pacific Society of Neurology and Psychiatry, held April 10 and 11, 1953, the following officers were elected for the coming year: president, Gordon Hutton, Vancouver, B. C., Canada; president-elect, William Baker, Seattle; secretary-treasurer, Robert A. Coen, Portland, Ore. The executive committee is Gerhard B. Haugen, Portland, Ore.; D. E. Alcorn, Victoria, B. C., Canada; Robert S. Dow, Portland, Ore., and Donald E. Stafford, Seattle.

CORRECTION

In the report of the transactions of the New York Neurological Society and the New York Academy of Medicine, Section of Neurology and Psychiatry, published in the March 1953 issue, Dr. C. Rosenheck's initials (page 397) were incorrectly given as H. R.

In the transactions of the December, 1952, meeting of the Philadelphia Neurological Society, published in the April issue of the ARCHIVES, the second line of the second paragraph of Dr. Walter Freeman's discussion, on page 531 should read as follows: "The overall mortality is 3.6% for prefrontal lobotomy, as against 1.7% for transorbital lobotomy."

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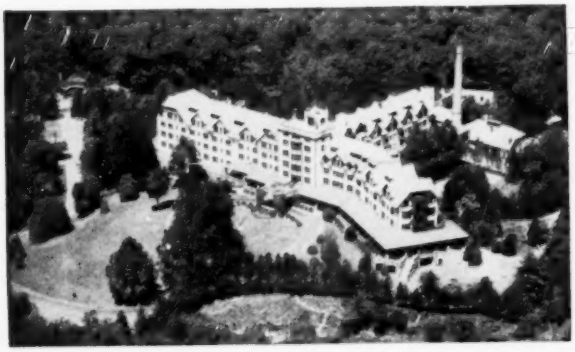

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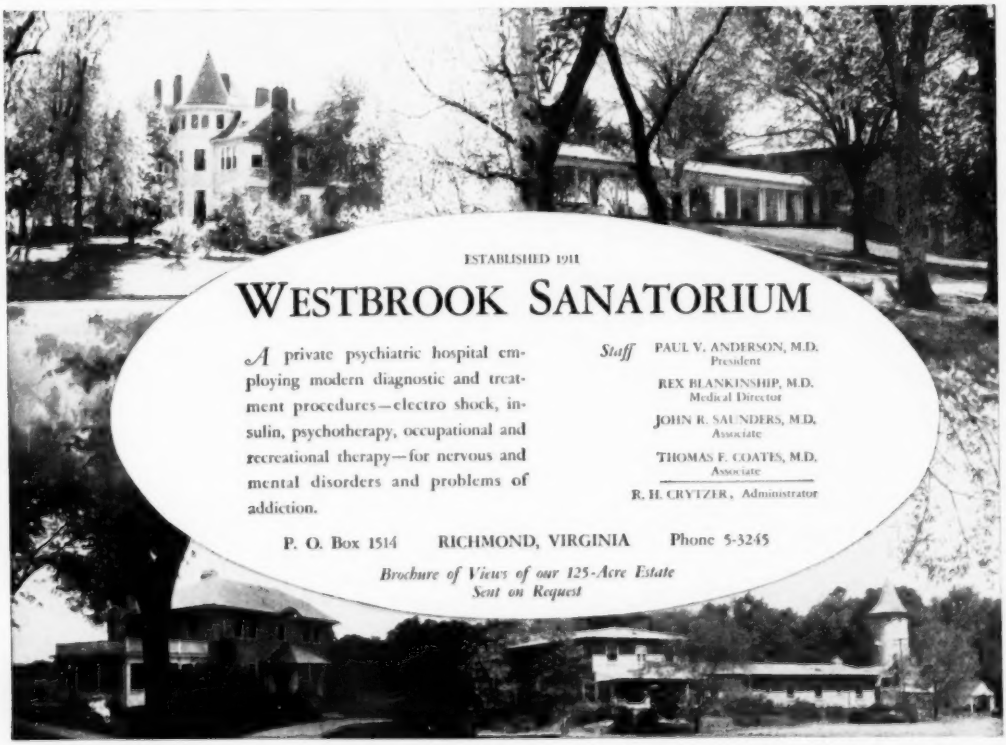

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